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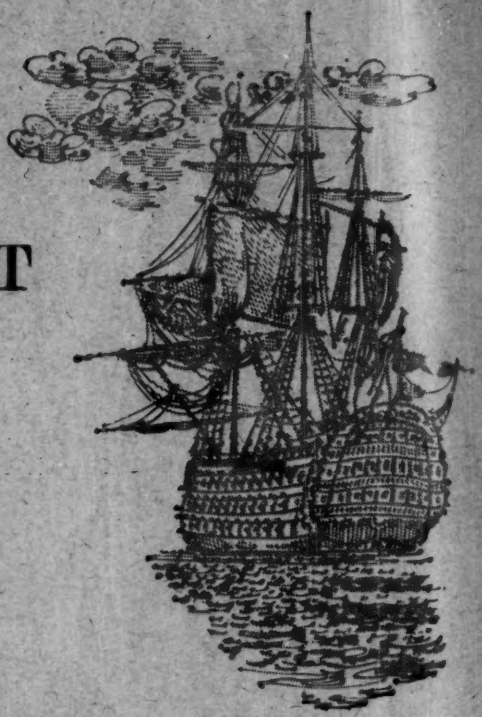

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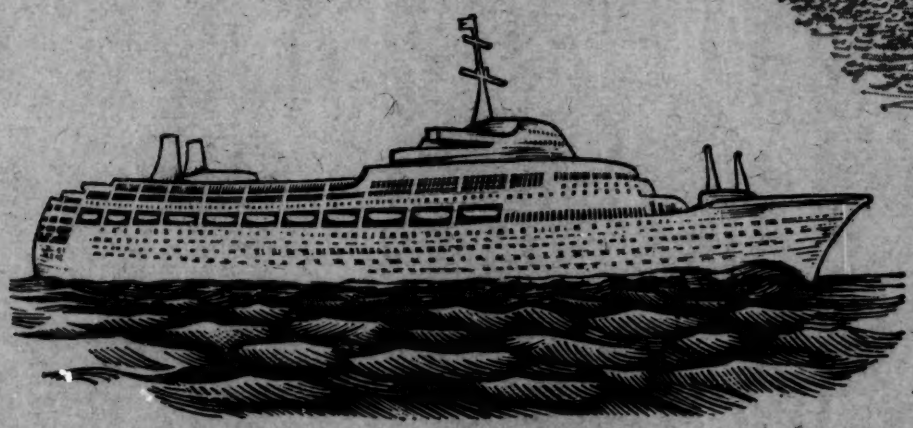

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 10 1961

A NEW VIEW OF ADRENERGIC NERVE FIBRES, EXPLAINING THE ACTION OF RESERPINE, BRETYLIUM, AND GUANETHIDINE*

BY

J. H. BURN, M.D., Hon.Sc.D., F.R.S.

Oxford

It is scarcely too much to say that our ideas of the sympathetic control of vascular tone are undergoing a revolution at the present time. At the beginning of this century Elliott (1904) put forward the suggestion that a post-ganglionic sympathetic fibre might transmit its impulse by liberating adrenaline. That suggestion has been generally accepted, with the reservation that the transmitter might not be adrenaline itself but something closely related to it. During the years 1920 to 1937 Cannon and his colleagues established this mode of sympathetic action, and Euler (1948) and Peart (1949) finally showed that the transmitter was for the most part noradrenaline. The picture seemed to be complete, and the matter seemed to be settled.

The Perfused Vessels of the Dog Leg

Almost by accident I made some observations 30 years ago which were not explained by this simple scheme. I had been introduced to perfusion experiments by Sir Henry Dale and had seen their usefulness in analysing the action of histamine. In 1928 the Dale–Schuster pump became available, and I set out to study the effect of stimulating the sympathetic fibres on the vessels of the dog hindleg. The blood was pumped into the femoral artery, and was collected from the femoral vein. A second pump then drove it through the lungs, and then it went back to the leg. To set up the perfusion with the use of only one dog rather than two, it was necessary to leave the hindleg without a circulation for about 45 minutes. When the perfusion began, the tone in the hindleg vessels was very low, and therefore adrenaline was added drop by drop to the blood in the venous reservoir to bring the tone up to its normal level. I then observed the effect of stimulating the post-ganglionic fibres in the lumbar sympathetic chain, and saw that it caused, not vasoconstriction, but vasodilatation.

Vasodilatation was often the only response obtained throughout an experiment, but, in some experiments, after an hour or two the response changed to vasoconstriction. It was usually true that brief stimulation, for three seconds only, caused vasodilatation, while in the later stages of an experiment a longer stimulation for 30 seconds caused vasoconstriction. It appeared that the longer the time during which adrenaline was added to the blood the more likely was stimulation to cause vasoconstriction, and I came to the conclusion that "if sympathetic stimulation releases adrenaline, then a store of adrenaline is required at the sympathetic nerve endings ready for release." I thought that in my experiments this store must have been destroyed during the period in which the hindleg vessels were without a circulation, and that with the addition of adrenaline to the blood the store was gradually replenished (Burn, 1932).

Later work showed that the vasodilatation caused by sympathetic stimulation was due to the release of acetylcholine, and indicated that there were cholinergic fibres in the lumbar sympathetic chain (Bülbring and Burn, 1935). This work did not, however, explain why cholinergic fibres were unaffected by a period of anoxia which put the adrenergic fibres out of action.

Noradrenaline in Organs

After Euler had found that noradrenaline was present in sympathetic nerves, and had suggested that it was the transmitter, Schmiterlöw (1948) demonstrated that noradrenaline was present in the walls of the blood-vessels, and Euler and Purkhold (1951) demonstrated that noradrenaline was present in the spleen, the liver, the kidney, and the salivary glands. Goodall (1951) also demonstrated that it was present in the heart. Moreover, this noradrenaline disappeared from the organs when the sympathetic nerves degenerated, and Euler therefore concluded that the noradrenaline in the organs must be located in the terminations of the sympathetic nerves themselves.

Action of Reserpine

The beginning of recent developments can be traced to the observation of Bertler, Carlsson, and Rosengren (1956) that when a large dose of reserpine was given by intravenous injection to a rabbit, and the rabbit was killed 16 hours later, the heart no longer contained any noradrenaline. Whereas normal rabbit hearts contained 1.57 μg./g., hearts from rabbits injected with reserpine contained only 0.03 μg./g. Later Burn and Rand (1957) showed that the injection of reserpine had a similar effect on the noradrenaline in the wall of the thoracic aorta, both in the rabbit and in the dog. They also examined the effect of stimulating the lumbar sympathetic on the perfused vessels of the dog's hindleg. In these experiments the perfusion began at the moment of stopping the natural circulation, so that in a normal dog stimulation always caused the expected vasoconstriction.

However, when the dog had been given reserpine on the two preceding days, stimulation caused dilatation as in my 1932 experiments; the dilator effect was abolished in the presence of atropine, and was due to acetylcholine. Since the sympathetic transmitter is known to be mainly noradrenaline and not adrenaline,

*A lecture delivered to the Plymouth Medical Society on April 14, 1961.

noradrenaline was added drop by drop to the venous reservoir, 0.5 mg. being added to 1 litre of blood. The noradrenaline caused vasoconstriction, but when no more was added the constriction gradually disappeared, and the tone in the vessels returned to the initial level. When sympathetic stimulation was applied at this point vasoconstriction was produced. Thus it was learnt that sympathetic stimulation caused vasodilatation, and was unable to cause vasoconstriction when there was no store of noradrenaline in the vessel walls, and it was also learnt that an infusion of noradrenaline restored the power to cause vasoconstriction (Burn and Rand, 1958a). This evidence confirmed the view put forward in 1932, which has already been quoted.

From the physiological point of view it was important to know whether the effect of noradrenaline in restoring the constrictor effect of sympathetic stimulation applied only when the animal had been given reserpine. Was the effect of an infusion of noradrenaline one which could be produced in the perfusion of normal vessels? We found that the effect was readily seen in normal vessels, though the increase was of short duration. Longer-lasting effects were obtained when we made plethysmograph records of the leg volume of dogs anaesthetized with chloralose. Having recorded the effect of stimulating the lumbar sympathetic chain, using stimuli of varying strengths, we gave an intravenous infusion of noradrenaline, and when the infusion was complete (the amount infused varying from 0.25 to 0.5 mg.) we waited until the direct effect of the noradrenaline had passed off. Stimuli of a strength which previously had no effect now produced vasoconstriction, and the smallest effective stimulus was in some experiments reduced to one-sixth of its previous value (Burn and Rand, 1960a).

Effect of Variation in the Store

The results indicated that the effect of an impulse passing along a post-ganglionic sympathetic fibre varied greatly according to the size of the store of noradrenaline present at the nerve ending. It is therefore evident that the action of reserpine in lowering the blood-pressure is due to the reduction of the store of noradrenaline in the vessel walls and in other organs such as the heart and spleen. When the patient is given reserpine the amount of noradrenaline in the sympathetic nerve endings is reduced, and therefore the impulses passing down the sympathetic nerves cause less vasoconstriction.

Direct evidence that the infusion of noradrenaline increased the amount of extractable noradrenaline was obtained by Pennefather and Rand (1960) for the kidney and for the horn of the uterus. They used these organs because they are paired. Evidence was also obtained by Whitby, Hertting, and Axelrod (1960) for the spleen and for the heart, using radioactive noradrenaline.

It is likely that in those who are subject to emotional crises there will be a larger output of noradrenaline from the adrenal medulla than in others. This larger output will fill the stores at sympathetic nerve endings and may thus be responsible for a higher level of blood-pressure.

Bretylium

A second substance, which was introduced as a hypotensive agent in 1959, is bretylium. The forerunner of bretylium was choline 2,6-xylyl ether bromide, which was synthesized by Hey (1952) in Leeds, and was shown by Exley (1957) to prevent the release of noradrenaline when post-ganglionic sympathetic fibres were stimulated. The blocking action of bretylium has been thought to be due to a local anaesthetic action on the nerve fibres, and Boura and Green and their colleagues (1960) have found that radioactive bretylium was taken up in greater amount by sympathetic ganglia than by other ganglia, and in greater amount by adrenergic nerves than by cholinergic nerves. Thus Boura and Green supposed that bretylium acted by preventing the conduction of impulses along the sympathetic post-ganglionic fibres. The action has, however, been located by Exley and Fleming (1960) on the terminal portion of these fibres rather than along their course.

The work of Burn and Rand (1960b) led them to support the conclusion of Exley and Fleming and to give it a more precise form. They were interested in the curious observation that many sympathetic effects were produced in the body by nicotine and by acetylcholine in the presence of atropine, in circumstances in which nicotine and acetylcholine were acting beyond the location of sympathetic ganglia. An example of this is given by the vessels of the rabbit ear. When the fibres from the superior cervical ganglion are stimulated the vessels constrict. They also constrict when a small quantity of nicotine is injected into the fluid perfusing the vessels, or when, in the presence of atropine, a small quantity of acetylcholine is injected. If the ear is taken from a rabbit previously given reserpine, then stimulation of the sympathetic fibres does not cause constriction, and likewise the injection of nicotine or of acetylcholine does not cause constriction (Burn and Rand, 1958b). From this it was evident that the constriction caused in the normal ear by nicotine or by acetylcholine was due to the release of noradrenaline, just as was the constriction caused by sympathetic stimulation.

The striking similarity in the action of acetylcholine and in the action of sympathetic stimulation both in the effect they produce and in the way of producing it is not confined to the rabbit-ear vessels. Thus it is seen in the isolated atria of the rabbit heart, where, in the presence of atropine, acetylcholine causes acceleration of the rate, but not when the atria are taken from a rabbit which has been treated with reserpine. It is also seen in the pilomotor response of the cat's tail. This can be studied by removing most of the hair of the cat's tail with clippers, leaving a series of tufts. Stimulation of the lumbar sympathetic chain causes the tufts to erect. The injection of acetylcholine into the skin at the base of a tuft also causes that tuft to erect. We found that noradrenaline was present in the skin of the cat's tail; when a cat was injected with reserpine the noradrenaline in the skin of the tail was greatly reduced. When a cat was injected with reserpine the injection of acetylcholine into the skin at the base of a tuft had almost no effect in causing erection of the tuft (Burn, Leach, Rand, and Thompson, 1959).

Another situation where similar observations were made was in the colon of the rabbit, after a portion of the colon was removed from the freshly killed animal, together with the extrinsic nerves, and was suspended in a bath. Sympathetic stimulation caused inhibition of the pendular movements, and the addition of a low concentration of nicotine to the bath had the same effect. If the rabbit had been injected with reserpine, however, both sympathetic stimulation and nicotine lost their inhibitory action (Gillespie and Mackenna, 1959).

Thompson (1958) has described a preparation of the cat's nictitating membrane which can be set up in a bath with its sympathetic supply. Stimulation of the sympathetic fibres causes contraction of the smooth muscle of the membrane, and so also does addition of nicotine to the bath. When a cat has been injected with reserpine the isolated nictitating membrane no longer contracts on sympathetic stimulation or on the addition of nicotine to the bath.

The noradrenaline which can be extracted from an organ with a sympathetic supply disappears not only when the animal is injected with reserpine but also when the nerves degenerate (Euler and Purkhold, 1951). Stimulation of the sympathetic fibres causes contraction of the spleen, and so also does injection of acetylcholine into the splenic artery. However, when the sympathetic fibres degenerate, injection of acetylcholine into the splenic artery no longer causes contraction of the spleen (Daly and Scott, 1961). When a cat was treated with reserpine, stimulation of the sympathetic fibres no longer caused contraction of the spleen and the amount of noradrenaline in the spleen was found to be greatly reduced.

In the six examples which have been given the same curious parallelism was found. Sympathetic stimulation caused effects which were mimicked by acetylcholine (in the presence of atropine) or by nicotine. These effects were no longer seen in animals treated with reserpine or in organs to which the sympathetic fibres had degenerated. Thus it appeared that sympathetic stimulation acted by liberating noradrenaline from the store (probably in the nerve endings), and acetylcholine or nicotine also acted by liberating noradrenaline from the same store. What was the meaning of this common action? Did it mean that the sympathetic nerves liberated acetylcholine?

Cholinergic Fibres in the Sympathetic Nerves

The work of Brücke (1935) suggested that this might be so. He had shown that acetylcholine caused erection of the hairs of the tail as already described, the amount required being small, about 5 μg. But in addition he made the observation that when a larger amount was injected, such as 0.2 mg., 40 times greater, there was again a brief erection of the tuft, after which sympathetic stimulation was no more effective. The larger amount of acetylcholine had blocked sympathetic stimulation, though stimulation still erected adjacent tufts where acetylcholine had not been injected. Burn and Rand (1960b) confirmed these observations, which suggested that the sympathetic fibres to the cat's tail were cholinergic, and that the acetylcholine released by impulses passing down them caused a discharge of noradrenaline.

In other words, we had a new conception of an adrenergic mechanism. Hitherto an adrenergic nerve had been conceived as a nerve in which the impulse released noradrenaline directly. Now it appeared that a sympathetic nerve might be cholinergic, liberating acetylcholine, and that the acetylcholine might in turn release noradrenaline from a store. Such a mechanism might be blocked by a large dose of acetylcholine which would paralyse the effect of small amounts of acetylcholine released from the nerve.

The conception that post-ganglionic sympathetic fibres might in some cases be cholinergic was not new. Thus Dale and Feldberg (1934) showed that all the fibres to the sweat glands were cholinergic. Earlier than this, Euler and Gaddum (1931) had found that some fibres from the superior cervical ganglion to the vessels of the tongue were cholinergic; Bülbring and Burn (1935) showed that some fibres to the vessels of the dog's hindleg were cholinergic. Other examples were given by the nictitating membrane (Bacq and Fredericq, 1935), by the dog uterus (Sherif, 1935), and by the cat heart (Folkow, Frost, Haeger, and Uvnäs, 1948). But, except for the fibres to the sweat glands, cholinergic fibres in the sympathetic nerves were regarded as being mixed together with adrenergic fibres which were assumed to constitute the principal innervation.

Hence the idea put forward by Burn and Rand (1959), that cholinergic fibres might be part of an adrenergic mechanism, was a new idea which had not been previously considered. If adrenergic effects were obtained as a result of the release of noradrenaline by cholinergic fibres, the question was raised whether there were, in addition, adrenergic fibres in the hitherto accepted sense which liberated noradrenaline without the intervention of acetylcholine.

The Splenic Nerves

The first step towards deciding this was to see if cholinergic fibres could be demonstrated in the long post-ganglionic fibres running to the spleen and in those running from the superior cervical ganglion to the vessels of the rabbit ear.

When acetylcholine was injected intravenously into a cat which had been treated with reserpine the spleen dilated. When the splenic nerves were stimulated in such a cat the spleen did not constrict as it usually does, but dilated. This dilatation was evidently due to the liberation of acetylcholine, because it was greater in the presence of eserine (which is an anticholinesterase) and it was abolished by atropine. Brandon and Rand (1961) examined the perfused spleen in a cat which had been treated with reserpine, allowing the effluent from the vein to run over a strip of muscle from the guinea-pig ileum. Stimulation of the splenic nerves had no effect on the contractions of this muscle. However, when an anticholinesterase (neostigmine) was added to the perfusion fluid, stimulation of the splenic nerves was followed by contraction of the ileum. In the presence of atropine this contraction did not occur. The evidence clearly showed the presence of cholinergic fibres in the splenic nerves.

By similar methods the presence of cholinergic fibres was demonstrated in the post-ganglionic supply to the vessels of the rabbit ear, in the hypogastric nerves to the cat uterus, and in the post-ganglionic supply to the nictitating membrane of the cat.

Action of Bretylium

The evidence thus indicated that in all post-ganglionic sympathetic fibres some cholinergic fibres were present. How could it be determined whether these were only an admixture or whether they constituted the whole supply? At this point bretylium provided a guide. In the first place the chemical structure of bretylium suggested that it would be likely to act more in relation to acetylcholine than to noradrenaline. Then bretylium was found to block the action of acetylcholine on the isolated atria of the rabbit heart. As already described, in the presence of atropine, acetylcholine quickens the

rate and force of the atrial beat. Bretylium blocked this action in the same concentration as it blocked the action of sympathetic stimulation (Huković, 1960). Then bretylium was found to block the action of acetylcholine (in the presence of atropine) in causing constriction in the vessels of the perfused rabbit ear, and it blocked the constriction caused by nerve stimulation in the same concentration.

Thus the evidence suggested that the action of bretylium was indeed exerted on the nerve terminations as Exley and Fleming had found, and that specifically it blocked the action of the acetylcholine liberated by the cholinergic fibres, so that it could not release noradrenaline. Now, since bretylium blocked the whole of the post-ganglionic sympathetic supply to the atria and to the rabbit-ear vessels, it followed that not merely some but all of these fibres were cholinergic. The earlier view was that bretylium prevented the release of noradrenaline. But tyramine is an agent which releases noradrenaline from the store at the sympathetic nerve ending by a direct action on the granules containing noradrenaline (Schümann, 1961). It was observed that, when bretylium blocked the release of noradrenaline by sympathetic stimulation, the effect of tyramine was not only undiminished but was increased (Burn and Rand, 1960b). Thus bretylium appeared to be an agent which prevented the acetylcholine coming from cholinergic fibres from liberating noradrenaline from the store, without interfering with the action of tyramine on the store.

At each of the sites where acetylcholine acts the blocking agents differ. Thus at the termination of the parasympathetic nerves the blocking agent is atropine. At the neuromuscular junction the blocking agent is tubocurarine. At sympathetic and parasympathetic ganglia the blocking agent is hexamethonium. Now we have a fourth site, at the terminations of the post-ganglionic sympathetic fibres, where the blocking agent is bretylium.

Action of Hemicholinium

This was the picture in July, 1959, when Rand and I parted company, he going to Sydney and I into retirement. When in Sydney, Rand became interested in the action of hemicholinium, a substance introduced by Long and Schueler (1954). The essential feature of the action of hemicholinium was discovered by MacIntosh, Birks, and Sastry (1956) in Montreal. They showed that it interfered with the formation of acetylcholine. They perfused the superior cervical ganglion, and collected the venous effluent, estimating the acetylcholine present in it. The addition of hemicholinium to the perfusion fluid did not alter the amount of acetylcholine in the venous effluent so long as the preganglionic fibres were stimulated at a slow rate; but, when the rate was faster, hemicholinium reduced the amount of acetylcholine leaving the ganglion and reduced the transmission of impulses through the ganglion. Both the defect of transmission and the fall in the outflow of acetylcholine were made good by the addition of choline to the perfusion fluid. MacIntosh and his colleagues demonstrated that the synthesis of acetylcholine by brain tissue was diminished by hemicholinium, but that the synthesis returned to its normal rate when choline was added.

Chang and Rand (1960) tested the effect of hemicholinium in a series of isolated preparations in which the sympathetic nerves could be stimulated. They used the hypogastric nerve to the vas deferens of the guinea-pig; the hypogastric nerve to the rabbit uterus; the sympathetic supply to the rabbit colon; the sympathetic supply to the vessels of the rabbit ear; and the sympathetic supply to the cat atria. With each of these preparations they obtained evidence that the effect of stimulation of the sympathetic fibres was blocked in the presence of hemicholinium, but was restored when the hemicholinium was removed or when choline was added. With the preparation of the vas deferens they were able to show that the inhibitory effect of hemicholinium was evident only when the rate of stimulation was fast. In addition they tested the effect of hemicholinium on the pilomotor response in the cat's tail to sympathetic stimulation. They found that when hemicholinium was injected into the skin at the base of the tufts, then during stimulation those tufts were slower in erecting and quicker in falling back.

Thus Chang and Rand found that in six preparations with a sympathetic innervation hemicholinium blocked the effect of stimulation in the same way as it blocked the effect of stimulating the phrenic nerve on the rat diaphragm. This indicated the existence of a cholinergic transmission at the terminations of the sympathetic post-ganglionic fibres. Since the block of stimulation was usually complete, and always nearly complete, the observations indicated that the innervation was not only cholinergic in part but was entirely cholinergic.

Location of the Store

The conception of the adrenergic nerves has hitherto been founded on the evidence that noradrenaline is present in the nerves (Euler, 1948) and is released on stimulation (Peart, 1949). Schümann (1956) discovered that dopamine, the precursor of noradrenaline, is present in the nerves, and Holtz and Westermann (1956) found that the enzyme dopa-decarboxylase, which converts the amino-acid dopa into dopamine, is present in the nerves. In view of these observations, how is the suggestion of a cholinergic mechanism to release the noradrenaline to be envisaged?

This question can only be settled with the help of the histochemists and the electron microscopists; thus work has recently been done by Abrahams, Koelle, and Smart (1957) on the nerve fibres running from the supraoptic nucleus to the posterior lobe of the pituitary body. Staining showed that these fibres contained acetylcholinesterase, and that therefore they were probably cholinergic. Now this tract of nerves has been examined by Gerschenfeld, Tramezzani, and De Robertis (1960), using the electron microscope, and they observed the presence in the fibres of secretory granules, which increased in size towards the terminations of the fibres, from a diameter of 600 Å in the middle of the fibres to a diameter of 1,500 Å near the endings. These granules probably contained vasopressin, for when examined in a dehydrated animal those at the endings had disappeared. At the nerve endings, however, there were in addition synaptic vesicles of a diameter of 400 Å, similar to those found in sympathetic ganglia. Both Koelle and his colleagues and De Robertis and his colleagues have put forward the suggestion that, within a single fibre, a nerve impulse might release a transmitter (acetylcholine) from synaptic vesicles, and that this transmitter might in turn release vasopressin from the secretory granules. If this suggestion were to be proved correct, then a similar situation might be found in the

sympathetic post-ganglionic fibres, where acetylcholine might release noradrenaline from the same fibre.

Action of Guanethidine

It remains to describe the action of guanethidine. From what has been said in explaining the action of reserpine and of bretylium, it is easy to explain the action of guanethidine. This substance appears from present evidence to be the best of the three substances for the control of hypertension. Guanethidine, like reserpine, has the property of releasing the stores of noradrenaline in the walls of the arteries, in the heart, and in other organs possessing a sympathetic innervation. The disadvantage of reserpine, however, is that it enters the brain, and produces effects there by reducing the stores of noradrenaline and of hydroxytryptamine. The patient becomes depressed and may even suffer from melancholia. With guanethidine these effects on the brain are not seen. It is a strongly basic substance which does not pass the blood–brain barrier. The main value of guanethidine therefore is that it acts like reserpine in the periphery but has no effect on the brain.

This, however, is not the only action of guanethidine, though it is the most important one. In addition, guanethidine has an action like that of bretylium on sympathetic post-ganglionic nerve endings. Thus, when tested on the isolated preparation of the vas deferens, guanethidine, like bretylium, blocks the effect of sympathetic stimulation, and this is seen long before there is a decline of the amount of noradrenaline present in the vas deferens. Whether this blocking action is of clinical importance is not certain. Guanethidine finally has some action which resembles, superficially at least, the peripheral action of cocaine. When injected into a spinal cat, guanethidine causes a moderate though prolonged rise of blood-pressure and a sustained contraction of the nictitating membrane. The effect of noradrenaline is then increased and the effect of tyramine is depressed. Thus in the spinal cat the immediate effect of guanethidine is very like that of cocaine (Burn and Robinson, 1952).

Conclusion

The evidence that all sympathetic post-ganglionic fibres release acetylcholine, which in turn releases noradrenaline, is weighty, but for a conception of such importance cannot be regarded as complete; that is to say, it provides a working hypothesis which must be tested by further observations. The hypothesis affords a very satisfactory explanation of the observations in the perfused hindleg which were made in 1932 and again recently. However, further work is required on the mechanism of vasoconstriction following sympathetic stimulation in skin vessels, in particular those of the perfused rabbit ear. For it may be that there is here and in other places a direct release of noradrenaline without the intervention of acetylcholine. Dilatation of skin vessels has not yet been obtained experimentally, though it is easy to produce in muscle vessels. It seems likely, however, that such a dilatation is seen in the skin when a young lady blushes, and that this blush is due to the direct effect of acetylcholine.

Summary

The current conception of the adrenergic nerve fibres is that the nerve impulse releases mainly noradrenaline from the nerve ending. Recently evidence has accumulated that the nerve fibre may first release acetylcholine, and that this acetylcholine then releases noradrenaline. This action of acetylcholine is nicotine-like, and not muscarine-like, and therefore is not abolished by atropine.

The noradrenaline present in the sympathetic post-ganglionic fibres is reduced in amount when the animal is treated with reserpine or with guanethidine. When the noradrenaline is reduced, the effect of sympathetic impulses is diminished. This reduction appears to account for the hypotensive action of reserpine and of guanethidine. Guanethidine has the advantage over reserpine in that it does not affect the brain.

The amount of noradrenaline which is released by a sympathetic impulse is increased when a slow intravenous infusion of noradrenaline is given. It thus appears that the noradrenaline present in sympathetic fibres is not only synthesized there but also accumulates as a result of uptake from the blood.

Bretylium probably acts by blocking the action of the acetylcholine liberated by the nerve impulse, so that it cannot liberate noradrenaline. Guanethidine also has this blocking property.

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BED REST, SALICYLATES, AND STEROID IN RHEUMATIC FEVER

BY

E. G. L. BYWATERS, M.B., F.R.C.P.

AND

G. T. THOMAS, M.B., M.R.C.P.

From the Rheumatism Research Unit (M.R.C.), Canadian Red Cross Memorial Hospital, Taplow, Bucks

Bed rest has been an essential part of the treatment of rheumatic fever since 1877, when Sibson showed that there were fewer residual valve lesions in patients who had been so treated. Salicylates were introduced by Maclagan in 1876, and since then and until the advent of steroids have been accepted, together with bed rest, as routine in the treatment of the disease. Few would deny that bed rest is likely to be of benefit, on the basis of resting the body and thereby the heart and thus sparing a damaged or potentially damaged organ; and Taussig and Goldenberg (1941) showed that there was a higher incidence of valvular disease in patients who had refused it. The position regarding salicylates is less clear. All agree that the drugs are effective in controlling temperature and arthritis, but there is less agreement about their effect on the heart. Thus Coburn (1943) claimed that in high dosage they reduced the incidence of carditis, but this has been denied by others (Warren *et al.*, 1946). When steroids were introduced by Hench *et al.* (1949) it was hoped that they would minimize or prevent heart damage, but again there have been conflicting reports on their efficacy, and a detailed study of several hundred patients, some treated with salicylates and others with steroid, showed no significant difference between them (Co-operative Clinical Trial, 1955).

In the years 1948–50 we treated most of our patients with bed rest alone, for we were not convinced that salicylates were of value except for their effect on symptoms. In 1950–1 we took part in the Co-operative Clinical Trial above in which we used cortisone, salicylate, and A.C.T.H.; later, in 1951–2, we used salicylates and hormone in larger doses and for longer periods. The purpose of this study is to describe the course of the disease in patients treated by bed rest alone and to relate the degree of rheumatic activity to heart damage, to compare cases treated by bed rest with others given salicylates or steroid, and to assess the role of each of these three treatments—bed rest, salicylate, and steroid—in the management of the disease.

Bed-rest Series (1948–50)

During this period we treated 125 patients with bed rest and analgesics such as codeine or phenadoxone hydrochloride ("heptalgin") to control joint pain but without salicylate or steroid. Another 14 had courses of these drugs for 7 to 14 days with no demonstrable effect, and these 139 patients are discussed together. All were under 17 years of age and fulfilled the criteria for diagnosis of rheumatic fever as defined by Duckett Jones (1944); 80 were boys and 59 were girls; 69 were aged between 3 and 10 years and 70 between 11 and 16.

On admission to the unit all patients were put first into side wards, where they remained until they were well enough to be transferred to the main ward and their nose and throat swabs were known to be negative for β-haemolytic streptococci; any found to have positive swabs were given intramuscular penicillin. Prophylaxis with penicillin or sulphonamides was not used at the time. For the first few days, and if the temperature was raised or there was acute arthritis, pericarditis, or any other evidence of active carditis, they were kept at complete rest, being washed and fed (stage 1); later they were allowed to feed themselves (stage 2) and then to wash (stage 3). In most cases stage 3 was reached by the end of the first week of admission, and patients were then kept at this stage until there had been no signs of rheumatic activity for at least two weeks.

Patients were examined daily with special reference to carditis, arthritis, skin rashes (erythema marginatum), and nodules. Chest skiagrams for heart size were taken within the first few days if patients were well enough to be taken to the *x*-ray department; these were repeated every two months, or more often if changes in size were suspected. Many patients were also screened. A full electrocardiogram was taken on the day of admission. If any abnormality was detected the graph was repeated, sometimes daily, and standard leads were repeated as a routine every three weeks. The temperature (oral) and pulse were recorded four-hourly, and the sleeping pulse each night at about 2 a.m. The weight was measured weekly, using a weighing-chair. Blood samples were taken each week for sedimentation rate (E.S.R.) (Westergren); the haemoglobin was estimated on admission and once every three weeks thereafter; the white-cell and differential counts on admission and later as necessary. The antistreptolysin O titre (A.S.T.) was estimated on admission and then every three weeks.

Arthritis.—Most of the 139 patients presented with acute arthritis, often after infection of the upper respiratory tract; a few had only vague limb pains but nevertheless fulfilled the Duckett Jones's criteria for diagnosis. The total duration of arthritis in 52 patients admitted within 14 days of onset—who, if they had received salicylates before admission, had them for a maximum period of 13 days—is shown in Table I. In nearly half (44%) it was for seven days or less; in less than a quarter it persisted for more than a fortnight. Most patients with such persistent arthritis were over 10 years of age, showing the tendency for arthritis to last longer in the older age-groups.

Erythema marginatum occurred in 10% of all cases. In some it persisted for only a few days and in others it recurred off and on throughout the illness, even up to the time of discharge from hospital, long after the E.S.R. had returned to normal.

Nodules.—These were noted in 34%. They usually appeared after six to eight weeks of rheumatic activity, rarely before that time. They were found earliest and most often over the olecranon processes, where they might be preceded by thickening of the subcutaneous tissue ("prenodular thickening"). Other sites were the patellae, the malleoli, the scapulae, the tendons of the wrists, hands, and feet, the spine, and the scalp. Their duration varied greatly; they might disappear within a few weeks or persist long after all other signs of activity had subsided and be present at the time of discharge from hospital.

Other criteria of rheumatic activity—temperature, sleeping pulse, sedimentation rate, weight, and anaemia—are best considered in relation to the duration of the disease before admission. 65 had been seen within 14 days of onset and the other 74 after 14 days (Table I).

Temperature.—About half (52%) of the cases admitted within 14 days of onset had, as would be expected, raised temperature, but this persisted for only one week in the majority. Nevertheless a few had continuous fever for three weeks.

Sleeping Pulse.—The total number of weeks the sleeping pulse was raised on two or more occasions in any one week above 80, 90, 100, and 110 a minute was noted. Very few patients had a rate above 110, and in many of the younger ones it was persistently between 80 and 90. The figure of above 100 was therefore chosen as a convenient dividing-line. The sleeping pulse was above 100 twice or more in any one week in 36 of the 139 (25%), and in most of them for a total of three weeks or less (22 out of 36). Another and better way of expressing the sleeping pulse was the total number of weeks during which it was above the discharge level (assumed normal) after the temperature had returned to normal. On this basis, 53 (38%) had raised rates, and these persisted for more than three weeks in 35. Tachycardia occurred more often in the recent cases, but the difference was not marked (Table I). Though the group as a whole showed this low incidence of raised sleeping pulse there was always tachycardia in the most severe cases. Thus in four patients who died the sleeping pulse was persistently above 120 for at least two months before death (Fig. 1). No other cases in the series had quite such persistent tachycardia, though in two with severe attacks the sleeping pulse was above 110 for four and six consecutive weeks; both had recurring fever and high sedimentation rates during this time and pericardial effusions. Fig. 2 illustrates the course of the disease in one of these cases and shows how such activity can subside with bed rest alone. In a few the sleeping pulse was slow, below 60, even when there was some carditis. Such bradycardia was noted in 15% of all cases.

E.S.R.—An E.S.R. of 20 mm./hr. or more (Westergren) was taken as abnormal. The total number of weeks for which the E.S.R. was abnormal was counted for each case. Twenty-six cases did not have raised rates at any time, though four of them had been admitted within 14 days of onset. Of the remainder, the E.S.R. was raised for totals of 1–3, 4–9, and 10 or more weeks in similar numbers of cases (Table I).

Anaemia.—Anaemia that could be attributed to rheumatic activity and not to iron deficiency was uncommon. In some severe cases, however, the haemoglobin fell from normal to below 70% in a few weeks, to rise again as activity subsided.

Weight.—Marked loss of weight was observed in only the worst cases. Often, however, there was a failure to gain weight at a normal rate when rheumatic activity was present; later, as it subsided, normal weight increment occurred (Fig. 2). This rise in weight (provided heart failure could be excluded) was a very useful sign that activity was coming to an end.

A.S.T.—The antistreptolysin O titre was 200 or more in 85% of all patients and in 90% of those admitted within 14 days.

Carditis.—Two grades of carditis were distinguished, A and B. Twenty-five out of 139 patients had no abnormal clinical signs in the heart at any time, though in five of them the P–R interval was 0.18 second or more.

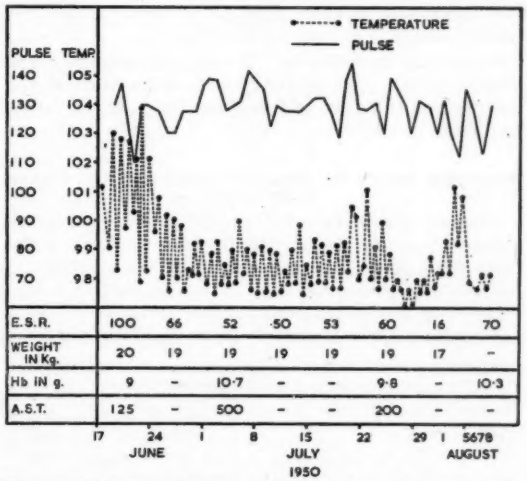

FIG. 1.—Persistent tachycardia above 120 in a child aged 7 who died after eight weeks in hospital.

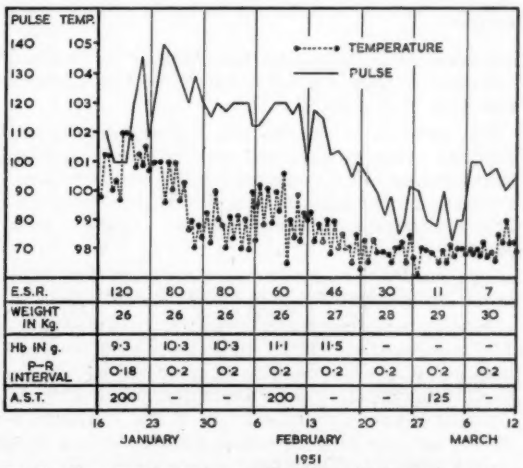

FIG. 2.—Treatment by bed rest. Sleeping pulse persistently above 110, raised temperature and E.S.R. for four weeks, and then subsiding activity with gain in weight (4 kg.).

TABLE I.—*Bed-rest Series (139 Patients). Duration of Rheumatic Activity*

Admission	No.	Arthritis (Days): Duration in 52 Cases Admitted Within 14 Days of Onset			Temperature				Sleeping Pulse						E.S.R. 20 mm./hr. or More (Westergren) for Total of			
					Above 99° F. on Admission	Days Remained Elevated			Above 100 in Any One Week			Raised Above Discharge Level			0	1–3	4–9	10+
		1–7	8–14	15+		1–7	8–21	22+	Total	1–3 Wks.	4+ Wks.	Total	1–3 Wks.	4+ Wks.	Weeks			
Total ..	139				59 (41%)	31 (22%)	8 (5%)	20 (14%)	36 (25%)	22 (15%)	14 (10%)	53 (38%)	18 (13%)	35 (25%)	26	38	37	38
Within 14 days	65	23 (44%)	18 (35%)	11 (21%)	34 (52%)	21 (32%)	3 (5%)	10 (15%)	18 (27%)	10 (15%)	8 (12%)	28 (43%)	12 (18%)	16 (25%)	4	25	16	20
After 14 days	74	—	—	—	25 (34%)	10 (15%)	5 (6%)	10 (13%)	18 (24%)	12 (16%)	6 (8%)	25 (33%)	6 (9%)	19 (24%)	22	13	21	18

Another 50 had soft (grade 1–2) diastolic murmurs at the mitral or aortic areas or both, transitory in 38 and constant in 12; the P–R interval was 0.18 second or more in a third. None of these 75 cases with minimal or no carditis had enlargement on *x*-ray examination. They were designated as cardiac group A. The other 64 (group B) had loud (grade 3 or more) murmurs on admission or developing shortly afterwards and persisting; some also had enlargement. Thirty-five were seen in first attacks of rheumatic fever; the other 29 had had previous rheumatic fever or chorea. The P–R interval was 0.18 second or more in 33%.

Pericarditis occurred in 15 cases—friction in 2 and effusion in 13. Four of the 13 with effusions developed heart failure and died, and were the only cases of failure and death in the series.

Relationship Between the Degree of Carditis and Other Features of the Attack

The sex distribution was similar in the two cardiac groups (A, nil or slight; and B, more marked)—rather more boys than girls in both. The age distribution, however, was different; most of the patients in A were aged 10 or less (62%), whereas in B most were over 10 (Table II). There was more often a family history of

TABLE II.—*Bed-rest Series. Sex and Age Distribution, and Incidence of Positive Family History*

Cardiac Group	No. of Cases	Sex		Age in Years on Admission		Positive Family History*
		M	F	1–10	11–16	
A	75	60%	40%	62%	38%	18%
B	64	54%	46%	36%	64%	30%

* History of rheumatic fever, chorea, or rheumatic heart disease in parents or siblings.

rheumatic fever, rheumatic heart disease, or chorea in parents or siblings in group B than in A—30% compared with 18% (Table II).

The duration of arthritis was analysed only in cases admitted within 14 days, and most of those in group B were admitted after 14 days (45 out of 64). There were therefore too few cases in group B with arthritis to make any comparison between the two cardiac groups possible.

The incidence of erythema marginatum was similar in the two groups—8% of A and 12% of B.

Nodules were much more frequent in B than in A—53% compared with 17%. In group A only 1 out of 25 with no carditis had nodules, as compared with 18% of those with transitory diastolic murmurs and 41% with constant diastolic murmurs. In B the incidence was similar in those with or without known previous attacks —54% and 52% (Table III).

TABLE III.—*Bed-rest Series: Incidence of Nodules*

	Total No. of Cases	No. with Nodules	% with Nodules
Cardiac group A	75	13	17%
No carditis	25	1	4%
Transitory grade 1–2 murmurs	38	7	18%
Constant ,, ,,	12	5	41%
Cardiac group B	64	34	53%
First attacks	35	19	54%
Second ,,	29	15	52%

The incidence of pyrexia, raised sleeping pulse, and raised E.S.R. in the two cardiac groups as a whole and in those cases admitted within 14 days is shown in Table IV. The incidence of all three was higher in

TABLE IV.—*Bed-rest Series: Percentage of Cases with Raised Temperature, Sleeping Pulse, and E.S.R.*

Cardiac Group	No. of Cases	Temperature Above 99° F.		Sleeping Pulse			E.S.R. 20 or More (Westergren) for Total of		
		On Admission	For 3+ Weeks	Above 100	Raised after Temperature Normal	Raised for 3+ Weeks	0–3	4–9	10+
							Weeks		
Total	139	41%	14%	25%	38%	25%	46%	27%	27%
A	75	33%	2·7%	14·8%	28·5%	12%	55%	29%	16%
B	64	53%	28%	39%	48%	39%	35%	23%	41%
65 Cases Admitted within 14 Days									
A	46	43%	2%	15%	35%	13%	54%	28%	17%
B	19	74%	47%	58%	63%	52%	21%	16%	63%

group B than in A, particularly in the 65 cases admitted within 14 days (46/75 of A and 19/64 of B). Thus in these recent cases there was continuous fever for more than three weeks in 47% of B and 2% of A; tachycardia, evidenced (*a*) by a raised sleeping pulse above 100 at any time in 58% of B and 15% of A, and (*b*) by sleeping pulse raised above discharge level for more than three weeks after the temperature was normal in 52% of B and 13% of A. Most cases in A had E.S.R.s raised for a total of three weeks or less (54%), whereas in 63% of B the E.S.R. was raised for 10 weeks or more.

Of the 65 patients admitted within 14 days of onset 56 were seen in their first attack of rheumatic fever, and any carditis was assumed to be new and recent: 46 were in cardiac group A (16 with no carditis and 30 with soft diastolic murmurs) and 10 in B (Table V). Per-

TABLE V.—*Bed-rest Series: 56 Patients Seen Within 14 Days of First Attacks: Numbers and Percentage with Raised Temperature, Sleeping Pulse, and E.S.R.*

Cardiac Status	No. of Cases	Temperature Raised for More than 3 Weeks	S.P. Raised for More than 3 Weeks after Temperature Normal	E.S.R. Raised for 10+ Weeks
Group A	46	1 (2%)	6 (13%)	8 (17%)
No carditis	16	0 (0%)	3 (19%)	0 (0%)
Grade 1–2 murmurs	30	1 (3%)	3 (10%)	8 (27%)
Group B	10	6 (60%)	7 (70%)	5 (50%)
Total	56	7 (12·5%)	13 (23%)	13 (23%)

sistent fever for more than three weeks was unusual in cases in group A and never occurred without clinical evidence of carditis, but was present in 6 out of 10 in group B. The E.S.R. was never raised for 10 weeks or more in patients without carditis, but was so raised in 27% of those with soft diastolic murmurs and in 50% of those in group B. Sleeping pulse raised above discharge level for more than three weeks after the temperature had returned to normal, though more common in B than in A, occurred as or more often in cases in group A with no carditis as in those with soft diastolic murmurs, and did not occur in 3 out of 10 with marked carditis in B.

Loss of weight and anaemia were uncommon and were seen only in group B cases. The incidence of raised A.S.T. was similar in the two groups—87% of A and 80% of B. In A there was no difference in incidence of raised A.S.T. in cases with no abnormal clinical signs (87%), with transitory diastolic murmurs (89%), or with constant diastolic murmurs (84%).

Thus the incidence of erythema marginatum and raised A.S.T. was similar in the two cardiac groups.

That of nodules was much higher in B than in A, and loss of weight and anaemia, both of which were uncommon, occurred only in the most severe cases of group B. Of the other criteria of activity, temperature, sleeping pulse, and E.S.R., all were more often abnormal in B than in A. Generally, E.S.R. and temperature were more closely related to carditis than sleeping pulse rates, but, as pointed out earlier, a prolonged raised sleeping pulse rate was invariable in the most severe cases and carried a bad prognosis. The four patients who died showed the following characteristics: loud murmurs and cardiac enlargement on admission in first attacks of rheumatic fever; nodules; pericarditis; and severe continued activity as judged by recurring temperature, E.S.R. between 40 and 100, and sleeping pulse rate above 110 for at least two months before death.

A striking feature of this study of the course of rheumatic fever in hospital in patients treated by bed rest alone was the short duration of activity in many cases. Thus arthritis persisted for a total of seven days or less in half the cases; only half had raised temperatures on admission which lasted for a week or less in the majority; only a third had sleeping pulse rates raised above discharge level after the temperature returned to normal; and in nearly half the cases the E.S.R. was raised above 20 mm./hour Westergren for a total of three weeks or less.

When the degree of carditis was related to rheumatic activity there was close correlation between carditis and nodules, prolonged raised temperature and E.S.R., but not with erythema marginatum or raised A.S.T. The sleeping pulse rate, though always raised to high levels in the worst cases, was as often raised in patients with no heart disease as in those with soft diastolic murmurs, and was sometimes normal in patients with recent carditis and loud murmurs. It is concluded, therefore, that nodules, prolonged raised temperature, and E.S.R. are usually better guides to prognosis than sleeping pulse rate, though in a few a persistently high sleeping pulse rate may portend a bad outcome. The outlook is worst, and death may occur, in patients with loud murmurs and cardiac enlargement in whom activity continues for two months or more, with recurring fever, high E.S.R., sleeping pulse rates above 110, nodules, and pericarditis.

Results of Treatment by Bed Rest Alone Compared with Treatment by Salicylate and Steroid

In 1950–1 we took part in the joint U.S.–U.K. trial (Co-operative Clinical Trial, 1955) and treated 86 patients with six-week courses of A.C.T.H., cortisone, or salicylate. All these patients were on prophylactic sulphonamide 1 g. daily. Of our bed-rest cases 89 would have qualified for treatment in the trial, as they were comparable in all respects; the other 50 included in the foregoing analysis fulfilled criteria for diagnosis but not for treatment, as they had only one minor criterion of activity (raised E.S.R.), whereas to qualify for treatment one major or two minor criteria were necessary.

We are grateful to Professor J. Knowelden, of the London School of Hygiene and Tropical Medicine, for part of the following analysis of the 86 trial cases and the 89 comparable ones treated by bed rest. The method of analysis is different from the one we used in the total bed-rest series of 139 patients but the same as in the report published by the Joint Committee (Co-operative Clinical Trial, 1955).

Arthritis.—29 of the joint trial cases and 40 of the bed-rest cases had arthritis on admission. The duration in the two groups is shown in Table VI. At the end of one week (day 8) 13.8% of the joint trial cases and 37.5% of the bed-rest series still had arthritis; two weeks later (day 22) these figures were 6.9% and 20%. After six weeks (day 43) 10% of both series had arthritis. There was then an increase in the proportion of cases with arthritis in the treated series, due to withdrawal relapse, but the proportion in the bed-rest series continued to fall.

TABLE VI.—*Joint Involvement at Start of Therapy at Specified Times*

Time from Start of Therapy in Days	U.S.–U.K. Trial (86 Cases)		Bed Rest (89 Cases)	
	No.	%	No.	%
1	29	100·0	40	100·0
2	18	62·1	34	85·0
3	14	48·3	33	82·5
4	14	48·3	24	60·0
5	11	37·9	23	57·5
6	10	34·5	21	52·5
7	6	20·7	15	37·5
8	4	13·8	15	37·5
15	3	10·3	9	22·5
22	2	6·9	8	20·0
29	2	6·9	6	15·0
36	1	3·4	4	10·0
43	3	10·3	4	10·0
50	6	20·7	2	5·0
57	4	13·8	1	2·5
63	1	3·4	—	—
13th week	1	3·4	—	—

Temperature.—57% of the bed-rest and 43% of the U.S.–U.K. trial cases had fever on admission, and this higher incidence of temperature in the bed-rest series continued until day 23 (Fig. 3). It was then similar in both until day 42, when there was an increase in the number of cases with fever in the treated series. At the end of nine weeks the incidence of raised temperature was again similar in the two.

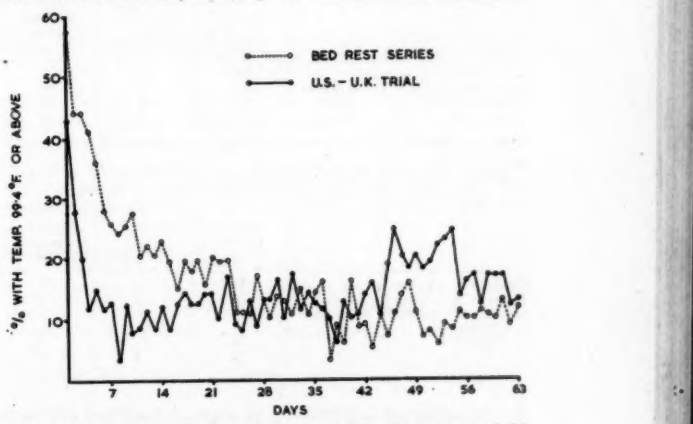

FIG. 3.—Percentage of 89 patients treated by bed rest and 86 treated in the U.S.–U.K. trial with raised temperature.

E.S.R.—In both series, nearly 90% of cases had rates of 20 or more on admission. Fig. 4 shows the percentage with raised E.S.R. in all the joint trial cases, in those of the joint trial treated by salicylates, and in the bed-rest series. The E.S.R. returned to normal more slowly in the bed-rest cases, but the level at 13 weeks was similar in all three groups.

Thus arthritis, raised temperature, and E.S.R. all tended to persist longer in the bed-rest than in the treated cases. Nevertheless the incidence of arthritis

was similar in the two by the sixth week, the temperature by the fourth week, and the E.S.R. by the eighth week.

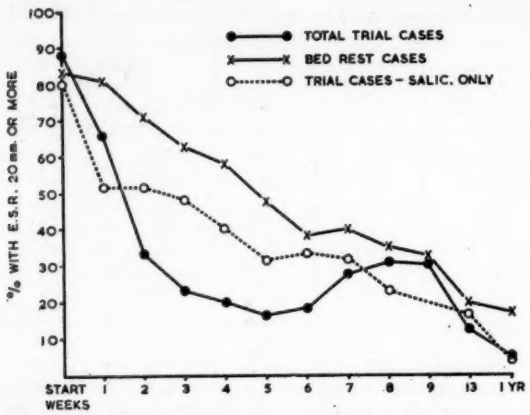

FIG. 4.—Percentage of 89 patients treated by bed rest and 86 treated in the U.S.–U.K. trial with raised E.S.R.

Carditis

Of the 175 cases, 42 had no carditis on admission (29 of the 89 in the bed-rest series and 13 of 86 in the U.S.–U.K. trial). Murmurs developed in hospital in 18 out of the 29 in the bed-rest series (Grade 1–2 in 16 and grade 3 in 2) and in only 2 out of the 13 in the trial (grade 1–2 in both) (Table VII). The remaining 133

TABLE VII.—42 *Cases with No Carditis on Admission*

	Total No. of Cases	U.S.–U.K. Trial (86 Cases)	Bed-rest Series (89 Cases)
No carditis on admission ..	42	13	29
Murmurs developed in hospital in	20	2	18
Grade 1–2	18	2	16
,, 3	2	0	2

TABLE VIII.—84 *Cases with Carditis on Admission in First Attacks: Number of Cases Reverting to Normal*

	Total No. of Cases	U.S.–U.K. Trial (86 Cases)	Bed-rest Series (89 Cases)
Carditis on admission	84	47	37
Reverted to normal in hospital ..	21	18	3
Grade of murmur that disappeared:			
Grade 1–2	20	17	3
,, 3	1	1	0

had carditis on admission; 49 of them had had previous attacks of rheumatic fever and carditis that could have been "old"—26 in the U.S.–U.K. trial and 23 in the bed-rest series; there was no difference in changes in cardiac status in hospital between the two groups. The other 84 had been admitted in first attacks with carditis that was assumed to be recent, 47 in the trial and 37 in the bed-rest series (Table VIII). Murmurs disappeared in hospital in 21 cases—in 18 out of the 47 in the U.S.–U.K. trial and in only 3 out of 37 in the bed-rest series. Of these 21 cases 20 had only minimal carditis evidenced by soft diastolic murmurs, but in one case in the U.S.–U.K. trial grade 3 murmurs disappeared. Five of the 84 with recent carditis died in hospital—4 of the 37 in the bed-rest series and only 1 of the 47 in the U.S.–U.K. trial. In none of the four in the bed-rest series that died had there been further demonstrable streptococcal infection to cause fresh rheumatic activity.

Comparison of the course in the two series shows that rheumatic activity subsided more slowly on all criteria in the bed-rest series, but the temperature was similar in both series by the fourth week, arthritis by the sixth week, and the E.S.R. by the eighth week. Fewer of the drug-treated cases developed murmurs in hospital and in more of them they disappeared. But this applied mainly to soft (grade 1–2) murmurs and may have little effect on prognosis, for in our experience few such cases subsequently develop serious heart disease. Nevertheless, four patients in the bed-rest series died and only one in the treated.

Thus by these various criteria the bed-rest series did worse, but no prophylaxis was used in this group and the two studies were not run concurrently. Further, we may have been dealing with a more severe form of the disease in the earlier series, since there was a higher proportion of cases with significant heart disease on admission: 59% with carditis had grade 3 murmurs as compared with 38% in the U.S.–U.K. trial.

A Third Series, Treated with Larger Doses of Cortisone and Salicylate

An analysis of cardiac status in the U.S.–U.K. trial cases 13 weeks after starting treatment and one year later showed no significant difference between those treated with cortisone, A.C.T.H., or salicylate (Co-operative Clinical Trial, 1955). A criticism of this trial has been that the dosage was too low and the duration of treatment too short, and that, if longer courses had been given, steroids might have proved more effective than salicylate. With this in mind, we treated a third series with 12-week courses of cortisone or salicylate in alternate cases.

Just as there had been less carditis on admission in the U.S.–U.K. trial cases than the bed-rest series, so in this third series there was less than in the U.K.–U.S. trial, again showing a tendency for the disease to become less severe over the years: this coincided with a fall in the overall incidence of notifiable rheumatic fever. Thus only 2 out of 26 patients with carditis on admission, all of whom had been admitted in first attacks within 14 days of onset, had grade 3 murmurs, as compared with 3 out of 13 in the U.S.–U.K. trial and 6 out of 15 in the bed-rest series admitted within a similar period. The patients in the new trial received 300 mg. of cortisone daily for two days, 200 mg. for five days, 100 mg. for six weeks, and then by weekly reductions to 25 mg. in the last and twelfth week, and salicylates on a body-weight basis in the form of calcium aspirin. During the stay in hospital no significant change occurred in the two cases with grade 3 murmurs. Of the other 24 with carditis on admission evidenced by grade 1–2 murmurs, similar numbers lost murmurs as in the U.S.–U.K. trial (16 out of 24—9 on salicylates and 7 on cortisone—as compared with 17 out of 29 in the U.S.–U.K. trial); and of the remaining 21 with no carditis on admission, 8 developed murmurs (5 on salicylate and 3 on cortisone) as compared with 2 out of 13.

We concluded, therefore, that longer courses of cortisone or salicylate have no advantage over the shorter ones used in the U.S.–U.K. trial, and that cortisone has none over salicylate in preventing or minimizing carditis, as evidenced by the development or disappearance of murmurs. The latter conclusion has been supported by the findings of the Combined Rheumatic Fever Study Group (1960) in America. Whether salicylate or cortisone therapy is more bene-

ficial during treatment in hospital than bed rest alone is difficult to assess, for the bed-rest and drug-treated series were not run concurrently, there was no prophylaxis in the bed-rest series, and more had serious heart disease on admission. Certainly the duration of rheumatic activity as judged by fever and E.S.R. was shorter in the drug-treated cases, and fewer developed murmurs and more lost them. This change applied, however, only to those with soft murmurs: there was no difference between the treatment groups in patients with grade 3 murmurs. Thus if steroid or salicylate influenced carditis in the development or disappearance of murmurs during hospitalization, it was only so far as grade 1–2 murmurs were concerned; and this, as has been pointed out, may have little effect on prognosis.

Four patients in the bed-rest series died in hospital, only one in the U.S.–U.K. trial, and none in the recent series treated with 12-week courses of salicylate and cortisone. Was this due to some beneficial effect of the drugs or to there being more severe cases in the earlier bed-rest series? The following features characterized the four fatal cases in this group: all were seen in first attacks with grade 3 murmurs and cardiac enlargement, and had rheumatic activity for minimum periods of eight weeks before death, with recurring fever, high sleeping pulse and sedimentation rates, nodules, and pericarditis. Signs of heart failure ultimately developed that did not respond to digitalis, mersalyl, and other measures. Two other cases in the bed-rest series had a similar degree of activity, but this subsided after five and six weeks' bed rest; both had pericardial effusions but not severe valve lesions. There were thus six patients with severe continued activity for five to six weeks, four of whom died in heart failure.

Were there any comparable cases in the drug-treated series? In the U.S.–U.K. trial there were four with this degree and duration of activity before the start of therapy; three were then given hormone (two A.C.T.H. and one cortisone) and the other salicylate. The three that were treated with hormone developed failure from sodium retention, but this responded to digitalis and mersalyl as activity was suppressed by the drug, and continued to subside after treatment had been stopped. All three made a good recovery and remained well over the next seven to eight years. The one that was given salicylates showed little response and the activity continued for many weeks, though the patient ultimately made a good recovery. Two other patients in the U.S.–U.K. trial and one in the third series were treated with salicylates within two weeks of admission, but then had recurring activity, for which they were given further courses of salicylate with little or no effect. One died in hospital; the other two were left with serious heart disease and died three and five years later.

Thus, of 13 patients in all three groups with continued or recurring activity and serious heart disease, three who were treated in the U.S.–U.K. trial with steroid made a good recovery; of four given salicylate (three in the U.S.–U.K. trial and one in the third series) one recovered, one died in hospital, and the other two were left with gross heart disease and died three and five years later; and of the six treated by bed rest, four died in hospital and two recovered. Treatment with hormone therefore appeared to be more effective than salicylate or bed rest alone.

Not only was salicylate ineffective in controlling activity in these cases, but there was reason to believe that it may have been harmful in three of them.

Thus in the one patient who died in hospital in the U.S.–U.K. trial, severe failure developed soon after the start of a fifth course of aspirin therapy. Treatment was changed 10 days later from aspirin to cortisone, but failure persisted and death occurred after another five weeks.

Another patient in this trial was treated with two courses of aspirin because of recurring activity. Failure developed shortly after the start of both of them and subsided on their withdrawal (Fig. 5). In the first course, 3 g. of acetylsalicylic acid was given daily. Two days later there

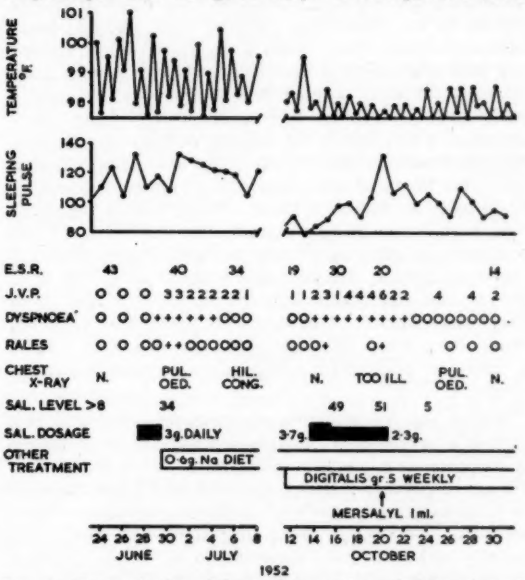
TEMPERATURE °F.
101
100
99
98
SLEEPING PULSE
140
120
100
80
E.S.R.
43 40 34 19 30 20 14
J.V.P.
0 0 0 3 3 2 2 2 2 1 1 1 2 3 1 4 4 4 6 2 2 4 4 2
DYSPNOEA
0 0 0 + + + + + + 0 0 0 0 0 + + + + + + + + + + 0 0 0 0 0 0 0 0
RALES
0 0 0 0 + + 0 0 0 0 0 0 0 0 + 0 + 0 0 0
CHEST X-RAY
N. PUL. OED. HIL. CONG. N. TOO ILL. PUL. OED. N.
SAL. LEVEL >8
34 49 51 5
SAL. DOSAGE
3g. DAILY 3·7g. 2·3g.
OTHER TREATMENT
0·6g. Na DIET
DIGITALIS gr.5 WEEKLY
MERSALYL 1ml.
24 26 28 30 2 4 6 8
JUNE JULY
12 14 16 18 20 22 24 26 28 30
OCTOBER
1952

FIG. 5.—Two episodes of heart failure after administration of aspirin. (Pul. oed. = pulmonary oedema. Hil. cong. = hilar congestion.)

was dyspnoea, the venous pressure was raised, and a chest skiagram showed pulmonary oedema. The drug was stopped and the patient put on a low-sodium diet (0.6 g./day) but no other treatment. The respiration rate and venous pressure returned to normal during the ensuing week and the skiagram then showed some congestion but no oedema. The second course of aspirin (3.7 g. daily) was given four months later, when the patient was on digitalis and low-salt diet. After two days there was some dyspnoea, with a rise in venous pressure; the dose was reduced to 2.3 g. daily. During the next six days dyspnoea persisted and the venous pressure continued to rise. The drug was then discontinued and mersalyl given, with clinical improvement. A chest skiagram still showed pulmonary oedema five days afterwards, but this cleared in another four days. In both episodes, therefore, failure developed within a few days of starting salicylate therapy and receded shortly after its withdrawal.

The third patient treated in the most recent trial developed pulmonary oedema soon after the start of two courses of "disprin," but this was controlled by salt restriction, digitalis, and mersalyl, and salicylate therapy was continued.

In two of the four patients in the bed-rest series who died there was also a suspicion that short courses of salicylate given towards the end of the illness might have been harmful.

In one there were signs of heart failure eight days before death that responded to digitalis. As failure improved there was a rise in temperature and E.S.R., and because of this salicylate 4 g. daily was given. After two days failure returned (salicylate level, 11 mg./100 ml.) and the patient died two days later.

The other was started on enteric-coated salicylate 4 g. daily because of continued activity. Three days later there

was sudden acute dyspnoea, with signs of consolidation of the right lung and death within eight hours, despite treatment with oxygen, morphine, digitalis, aminophylline, and penicillin. At necropsy there was typical rubbery consolidation of the whole of the right lung from rheumatic pneumonia.

All these patients who appeared to deteriorate on salicylate had had cardiac enlargement and active disease, and the drug had been given in the hope of controlling the activity. In those who survived it was ineffective in controlling activity but caused heart failure. In the others, death from heart failure, in one case with rheumatic pneumonia, followed shortly after starting treatment. The mechanism by which salicylates precipitate failure is not fully understood. Phear (1955) suggested it was due to the sodium content of salicylate and bicarbonate mixtures, but it has also been recorded with other forms of salicylate—that is, aspirin (Granville-Grossman and Sergeant, 1960). Other factors suggested have been increased plasma volume (Reid *et al.*, 1950) and increased plasma volume with pulmonary capillary damage (Sutcliffe, 1955); and Hetzel *et al.* (1959) have shown that salicylates can cause sodium and fluid retention. Raised cardiac output from the increased metabolism that salicylate induces (Cochran, 1954) is another possibility which should receive serious attention.

Before the introduction of hormone we found that persistent severe activity often precipitated heart failure in patients with cardiac enlargement, that this failure did not respond to digitalis, mersalyl, and other measures so long as activity persisted, and that sometimes death resulted. Salicylates were ineffective in controlling activity and sometimes appeared to do harm. Steroid, on the other hand, suppressed activity in similar cases treated in the U.S.–U.K. trial. Though the preparations used at that time (A.C.T.H. and cortisone) caused temporary failure from sodium retention, this responded to digitalis and mersalyl as the activity subsided, and the patients made a good recovery. Now we have drugs, such as prednisone, which cause little or no retention. Since they have been available we have used them in all patients with enlargement and marked activity; the activity has been controlled and failure has not developed. We have also used them in patients with failure and activity, again with control of the activity, the failure then responding to digitalis and mersalyl.

Conclusions

Our present views of the treatment of rheumatic carditis, based on experience of bed rest alone and short and longer courses of salicylate and hormone, are therefore as follows. The majority of cases with rheumatic fever to-day are mild and respond to bed rest alone; though salicylates may be helpful in relieving joint pains and other symptoms they do not significantly alter the course of the disease or the cardiac status. Steroids are not of proved value in these cases, for, though they may shorten the duration of rheumatic activity, there is no evidence that they benefit the heart, except possibly in the development or disappearance of soft diastolic murmurs in hospital; and a separate study has shown that this may have little effect on the prognosis five years later (unpublished data).

Steroids without a salt-retaining action are indicated, however, in all patients with cardiac enlargement and marked activity, for by suppressing the activity they lessen the risk of failure developing, or, if failure is already present, allow a satisfactory response to digitalis and mersalyl which otherwise might not occur. Salicylates do not adequately control activity and are potentially dangerous in such cases, since they may precipitate lung oedema or rheumatic pneumonia. Continuous prophylaxis is an essential background measure.

Summary

The course of rheumatic fever in hospital in patients treated by bed rest alone and not given prophylaxis has been studied, and the degree of carditis related to other features of the attack. Prolonged raised temperature and sedimentation rate were more closely related to carditis than the sleeping pulse, but in severe attacks persistent tachycardia was a constant feature and carried a poor prognosis. Anaemia and loss of weight were uncommon and occurred only in the worst cases. Nodules were rare without heart disease, but were present in a quarter of those with slight carditis and in half of those with severe carditis.

The course in hospital in some patients treated by bed rest has been compared with that in others who were given six-week courses of A.C.T.H., cortisone, or aspirin, together with prophylactic sulphonamide. The two groups were comparable in most respects, although (*a*) they were not run concurrently; (*b*) only the drug-treated series was given prophylaxis; and (*c*) the latter had less heart disease at the start. Arthritis, temperature, and sedimentation rate subsided more slowly in the bed-rest series, but the temperature was similar in the two by the fourth week, arthritis by the sixth week, and the sedimentation rate by the eighth week; the rapid subsidence of activity in some of the bed-rest cases was striking. There was little difference in changes in cardiac status in the two groups, except in the development or disappearance of soft (grade 1–2) murmurs, and this may have no important effect on the residual heart state five years later.

A third group of 47 cases was treated with 12-week courses of either cortisone or salicylate and did no better than those who had salicylate, cortisone, or A.C.T.H. for only six weeks.

Conclusions are drawn on the role of bed rest, salicylate, and steroid in the management of the disease. In many cases bed rest with salicylate to control fever and joint pain suffices, but in a few with severe attacks and cardiac enlargement delta-steroids are indicated and salicylates are potentially dangerous since they predispose to pulmonary complications.

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FIVE-YEAR FOLLOW-UP ON PATIENTS WITH RHEUMATIC FEVER TREATED BY BED REST, STEROIDS, OR SALICYLATE

BY

G. T. THOMAS, M.B., M.R.C.P.

Rheumatism Research Unit (M.R.C.), Canadian Red Cross Memorial Hospital, Taplow, Bucks

Many important studies on the cardiac sequelae in rheumatic fever have been published, notably by Ash (1948) and by Bland and Jones (1951). In both studies large numbers were followed for 10 years or more. Ash, in a study of 537 patients over 10 years, found that 59% had signs of heart disease after recovery from the initial illness and that the signs subsequently disappeared in 9% of them. The remaining 41% had no residual heart lesions, but signs developed later in a quarter, of whom 80% had had recurrences. Bland and Jones followed 1,000 patients for 20 years. As in Ash's series, over half had rheumatic heart disease at the beginning of the follow-up study; at 10 years 11% were normal and at 20 years 16%. A quarter of those without heart lesions at the start had developed cardiac damage by 10 years —"usually pure mitral stenosis"—and 44% at 20 years. Whereas Ash stressed the role of recurrences which had occurred in 80% of those that deteriorated, Bland and Jones did not always relate changes in cardiac status to recurrences or the total number of attacks.

The present study concerns 198 patients followed for a minimum period of five years and many for 6 to 10 years. All fulfilled the criteria for the diagnosis of rheumatic fever as defined by Duckett Jones (1944); 125 had been admitted in 1948–50, and comprised the bed-rest series, of whom 111 were treated in hospital with bed rest and analgesics such as codeine and the other 14 with A.C.T.H., cortisone, or salicylate for periods of 14 days or less without demonstrable effect. None of these 125 patients was given prophylactic penicillin or sulphonamide in hospital, though prophylaxis was instituted in any who subsequently had recurrences. The other 73 were admitted in 1950–1, and were treated with six-week courses of A.C.T.H., cortisone, or aspirin in the U.S.–U.K. trial (Co-operative Clinical Trial, 1955). All 73 were on prophylactic sulphonamide 1 g. daily in hospital, and the great majority continued to take the tablets regularly throughout the follow-up period.

Though the number of our cases is small, the cardiac findings have been considered in greater detail than in some of the earlier series, and due attention has been paid to the effect of recurrences and to the total number of attacks. The purpose is to describe any changes in cardiac status that occurred, to relate them to recurrences and the total number of attacks, and to show to what extent, if any, they were affected by treatment with hormone or salicylates, or by prophylaxis. Previously we had found that drug therapy was only occasionally of more benefit than bed rest alone in the acute phase of the disease (Bywaters and Thomas, 1961) and that prophylaxis was effective in reducing the number of recurrences in this country (Bywaters and Thomas, 1958), as had been the experience in the U.S.A. (Thomas and France, 1939).

Bed-rest Series (125 Cases)

All 125 patients were followed for five years and many for 6 to 10 years. At each follow-up examination (done at yearly intervals approximately two months from the date of admission), the patients were asked whether sore throats, rheumatism, or chorea had occurred during the preceding 12 months, and a note was made of their occupation and physical activities (games, cycling, dancing, etc.). In addition to a clinical examination, electrocardiograms (standard leads only unless cardiac enlargement known or suspected) and chest skiagrams for heart size were taken in all patients; many were also screened. Phonocardiograms were done on any that showed changes in heart signs. Weight, height, and temperature were recorded and blood was taken for sedimentation rate, packed cell volume, and antistreptolysin titre.

As has been stated, none were put on to prophylaxis while in hospital, and 19 out of the 125 had recurrences of rheumatic fever or chorea after discharge. Prophylaxis was instituted in those that had recurrences. The follow-up findings are considered in (*a*) the 106 that did not have recurrences, and (*b*) in the 19 that did.

106 Patients Without Recurrences

Of these 106 patients, 63 had no carditis or slight carditis during their original hospital stay: 22 had no abnormal clinical signs (P–R interval 0.18 second or more in five); and 41, soft (grade 1–2) diastolic murmurs (increased P–R interval in one-third). None had enlargement. The other 43 had more marked carditis—that is, grade 3 murmurs and often enlargement.

No Carditis or Slight Carditis (63 Cases)

All 22 patients with no abnormal clinical signs in the heart in hospital were normal at five years. Eight of them were seen for subsequent follow-ups at 6 to 10 years and remained normal.

Of the 41 patients with grade 1–2 diastolic murmurs, the murmurs were transitory in 32 and constant throughout the stay in hospital in 9. In 13 out of the 32 in the transitory group the murmurs were heard at the mitral area only, in 13 at the base only and in 6 at both areas. In some of them one or both murmurs were present only for the first few weeks after admission; in others they were heard on and off throughout the patients' stay in hospital; and in a few only towards the end of the illness when the patients were ambulatory. Adequate data on mitral systolic murmurs that might have accompanied transitory mitral diastolic murmurs were not available, for at that time little attention was paid to systolic murmurs unless they were maximal at the apex and of grade 3 or more intensity, and none of these patients had such murmurs. At five-year follow-up 4 of the 32 had signs of heart disease (a basal diastolic murmur of grade 1–2 intensity in each case) and 28 were normal. The four with murmurs were all followed subsequently: in two the murmurs persisted at six and eight years; in the other two they had disappeared at seven years. Of the 28 who were normal at five years, 20 were seen later and remained normal. Thus, of 24 patients with transitory murmurs in hospital who were followed for more than five years, 22 were normal and 2 had minimal carditis.

In the other nine patients with grade 1–2 murmurs the murmurs were present on admission or developed shortly afterwards and persisted; basal diastolic murmurs only in five, mitral diastolic murmurs in three, and both

murmurs in one. None had had previous rheumatic fever. At five-year follow-up there was evidence of carditis in six cases (basal diastolics in four and mitral systolics in two); the other three were normal. The six with carditis at five years were seen at subsequent follow-ups over periods of six to nine years, and the murmurs persisted in all of them. The three who were normal at five years were seen at eight and nine years and remained normal.

Thus none of these 41 cases with slight carditis in hospital evidenced by grade 1–2 diastolic murmurs developed serious heart disease during the period of follow-up, though 33 were seen at six to nine years. At five years only 10 out of 41 had carditis, usually evidenced by basal diastolic murmurs (in 8 out of 10 cases). The incidence of carditis was higher when the murmurs had been heard constantly in hospital (in six out of nine cases) than when they had been heard transitorily (in 4 out of 32 cases).

Conclusions.—Patients who have had rheumatic fever but no evidence of carditis or with a prolonged P–R interval only, and who do not have recurrences, have normal hearts when seen for follow-up at five years. Those who have had slight carditis evidenced by soft diastolic murmurs are usually normal at five years, but some still have soft murmurs, particularly if the murmurs were heard constantly in hospital. None developed serious heart disease.

More Marked Carditis (43 Cases)

These 43 patients had grade 3 murmurs (mitral systolic, mitral diastolic, or basal diastolic) on admission to hospital or developing shortly afterwards and persisting. Many also had enlargement. Eight had aortic incompetence only, 18 had mitral valve disease only, and 17 had both lesions. Twenty-four had been admitted in first attacks of rheumatic fever; the other 19 had had previous rheumatic fever or chorea. At five-year follow-up 30 were unchanged, 2 were normal, in 5 the signs were less, and in six they were more pronounced (Table I).

TABLE I.—*Five-year Follow-up in 43 Patients with Marked Carditis in Hospital and No Recurrences*

	No. of Cases	Signs Normal	Signs Unchanged	Signs Less	Signs More	Died
Total	43	2	30	5	6	0
1st attacks	24	2	15	4	3	0
2nd attack	19	0	15	1	3	0
Aortic incompetence in hospital:	8	0	8	0	0	0
1st attack	5	0	5	0	0	0
2nd ,,	3	0	3	0	0	0
Mitral valve disease in hospital:	18	2	15	0	1	0
1st attack	11	2	8	0	1	0
2nd ,,	7	0	7	0	0	0
Mitral and aortic lesions in hospital:	17	0	7	5	5	0
1st attack	8	0	2	4	2	0
2nd ,,	9	0	5	1	3	0

Of the 30 in whom the signs were unchanged, equal numbers had been seen in first and second attacks; 8 had had aortic incompetence only, 15 dominant mitral valve disease, and 7 both lesions. Though there was no change in clinical signs, in 12 there was some reduction of heart size on *x*-ray examination and in one some increase. Twenty-seven were followed after five years and no further change was noted.

The two patients who had no signs of heart disease at five years had been seen in first attacks with mitral-valve disease evidenced by mitral systolic murmurs. The systolic murmurs were not audible at the third and subsequent follow-ups to seven and eight years.

All five in whom the signs became less had had mitral and aortic incompetence. Four had been seen in first attacks. In two of them mitral incompetence had disappeared at two years but aortic incompetence persisted; the findings were unchanged at six and nine years. In the other two there was no aortic incompetence but still mitral incompetence at one year; the signs remained unchanged at eight years. The other had had previous rheumatic fever. At five years there was no evidence of mitral valve disease but still some aortic incompetence. One year later the aortic incompetence disappeared and the heart was normal.

Of the six in whom the signs were more marked, three had been seen in first attacks; one had mitral-valve disease only and the other five mitral and aortic incompetence. Three developed opening snaps in addition to mitral systolic murmurs, as possible evidence of some stenosis, two at three years and one at five years. In the other three there was increased aortic incompetence with enlargement of the left ventricles, though in one the mitral signs disappeared.

Conclusions.—In patients discharged from hospital with grade 3 or more murmurs there may be a regression of physical signs over a follow-up period of five years, particularly if there has been only one attack (six out of seven patients whose signs returned to normal or became less had only one attack as compared with 18 out of 36 who were unchanged or worse). The usual change is then the disappearance of slight aortic or mitral incompetence. Occasionally (6 out of 43 cases) the signs became more marked. Thus there may be increasing aortic incompetence, and opening snaps may develop in patients with mitral incompetence as possible evidence of early stenosis: frank mitral stenosis (snapping first sound, opening snap, and mitral diastolic murmur) did not occur.

19 Patients With Recurrences

Of these 19 patients, 15 had one recurrence of rheumatic fever, three had two or more, and one had three attacks of chorea. Eleven were seen for follow-up five years after their last attack, the other eight at two to four years. When last seen, four were normal, in three there had been no change in signs since the first admission, in three the signs were less, in seven they were more marked, and two had died (Table II).

TABLE II.—19 *Patients with Recurrences*

Cardiac Status in Hospital	No. of Cases	Cardiac Status at Follow-up				
		Normal	Signs Unchanged	Signs Less	Signs More	Died
Total	19	4	3	3	7	2
No carditis or grade 1–2 murmurs:	6	4	0	0	2	0
1st attack	5	4	0	0	1†	0
2nd or later attack	1	0	0	0	1*	0
Grade 3 murmurs:	13	0	3	3	5	2
1st attack	5	0	3	1†	1*†	0
2nd or later attack	8	0	0	2*	4 (3*)	2*(1†)

* 2–4 year follow-up. † More than 1 recurrence.

All four that were normal had had no carditis or slight carditis during their first admission, had been seen in first attacks and had only one recurrence (five-year

follow-up in all). The three in whom the signs were unchanged had had grade 3 murmurs in first attacks and only one recurrence (five-year follow-up). The three cases in whom the signs were less had all had mitral and aortic incompetence. One had been seen in a first attack, had two recurrences and only mitral incompetence when last seen at five years. The other two had had previous attacks and one recurrence; in one mitral and in the other aortic incompetence had disappeared at the last follow-up (five years in one and two to four years in the other).

Two of the seven in whom the signs were more marked had had only grade 1–2 murmurs in their first admission. One of them, seen in a first attack, had three recurrences of rheumatic fever and, later, mitral and aortic incompetence (five-year follow-up). The other, seen in a second attack with a soft basal diastolic murmur, had a recurrence at five years with a transitory mitral systolic murmur, and two years later had all the signs of mitral stenosis as well as slight aortic incompetence (two-year follow-up). The other five had had grade 3 murmurs in their first admission. One, who had been admitted in a first attack with aortic incompetence and a transitory mitral diastolic murmur, had three recurrences of chorea and, two years later, mitral stenosis (two-year follow-up). The other four had had previous rheumatic fever and only one recurrence. At the last follow-up there was increased mitral and aortic incompetence in one case (five-year follow-up), opening snaps had developed in addition to mitral systolic murmurs in two (two to four years in both), and there were signs of mitral stenosis (opening snap and mitral diastolic murmur) in the other, who had had only a mitral systolic murmur previously (two to four-year follow-up). Thus three of the seven ultimately had signs of mitral stenosis, which had not been observed in cases without recurrences.

The two patients who died had been admitted with grade 3 murmurs in second attacks. One had bacterial endocarditis at three years and the other died in failure from a second recurrence.

Conclusions.—Patients with no carditis or slight carditis in first attacks who have had only one recurrence may be normal at follow-up (four out of four cases), but with previous attacks or more than one recurrence serious heart disease may develop. Patients with grade 3 murmurs may be no worse after recurrences and the signs may even be less, despite more than one recurrence or histories of previous attacks. Often, however, the signs become more severe or the patients may die. Such deterioration occurs with more than one recurrence or with histories of previous attacks. The outlook after recurrences is therefore worse in patients with marked carditis who have had previous attacks or who have more than one recurrence.

Cardiac Status on First Admission to Hospital and at Follow-up in Relation to Total Number of Attacks of Rheumatic Fever

The cardiac status on first admission to hospital in 139 patients who originally comprised the bed-rest series, and at the last follow-up in the 125 who were seen at five years (four died in hospital and there were 10 defaulters at follow-up) in relation to the total number of attacks of rheumatic fever will now be considered.

Cardiac Status in Hospital (139 Patients).—25 had no signs of heart disease, 51 had grade 1–2 murmurs, and 63 had grade 3 murmurs during their first admission to this hospital (Table III); 107 had been seen in first attacks, the other 32 had had previous rheumatic fever or chorea. Of the 25 who were normal, 24 were admitted in first attacks, as were 48 out of 51 with grade 1–2 murmurs. Thus of a total of 76 with no carditis or slight carditis 72 were seen in first attacks. Of the 63 with more marked carditis on admission (grade 3 murmurs), on the other hand, half had had previous attacks, and of those admitted in attacks (32) the majority (28) had grade 3 murmurs. Thus there was good correlation between the degree of carditis and the number of attacks.

TABLE III.—*Cardiac Status on First Admission in* 139 *Patients in Relation to Number of Attacks of Rheumatic Fever*

	No. of Cases	Normal	Grade 1–2 Murmurs	Grade 3 Murmurs
Total	139	25	51	63
Admitted in 1st attack ..	107	24	48	35
Admitted in 2nd or later attacks	32	1	3	28

Status at Follow-up (125 Patients).—All 125 patients were followed for five years after discharge from hospital, and, as has been stated, 19 of them had recurrences during this period. Of the 19 with recurrences 11 were seen five years later, the other eight at two to four years. Thus 117 of the 125 patients were seen five years after their last known attack and eight at two to four years; 84 had then had one attack, 25 two, and 16 three or more; 59 were normal, in 43 the heart signs were unchanged, in 8 they were less, and in 15 they were more marked or the patients had died (Table IV). Of the 59 who were normal, the majority (52) had had one attack; where the signs were unchanged or less, similar numbers had had one or two or more attacks; but when the signs were more marked or the patients had died, most had had three or more (10/15). Looked at another way, with one attack 3 out of 84 were worse at follow-up; with two attacks, 2 out of 25; but with three or more attacks, 10 out of 16. Of 13 survivors who were worse at follow-up, five had questionable evidence of developing mitral stenosis (opening snaps in addition to mitral systolic murmurs); three had definite stenosis; three had increased aortic incompetence; and 2 had increased aortic and mitral incompetence. All three with mitral stenosis had had three or more attacks.

TABLE IV.—*Cardiac Status at Follow-up in* 125 *Patients in Relation to Total Number of Attacks of Rheumatic Fever*

	No. of Cases	Normal	Un-changed	Signs Less	Signs More or Death
Total	125	59	43	8	15
1 attack ..	84	52	25	4	3
2 attacks ..	25	6	16	1	2
3 or more attacks	16	1	2	3	10

Conclusions.—The degree of carditis on first admission to hospital is closely related to the previous history: in first attacks the majority of patients have no or slight carditis; in second or later ones, most have serious heart disease. In patients who are followed for five years after their last attack of rheumatic fever there is most likely to be deterioration in cardiac status or death in those who have had three or more attacks. The development of mitral stenosis seems to be closely related to the total number of attacks, as it was not observed except after three or more.

Comparison with Other Cases Treated with A.C.T.H., Cortisone, or Aspirin

Seventy-three patients were treated in this hospital with six-week courses of A.C.T.H., cortisone, and aspirin in the U.S.–U.K. Trial in 1951–52 (Co-operative Clinical Trial, 1955) and were followed for five years. All were given prophylaxis (sulphonamide 1 g. daily) in hospital, and most continued to take the drug regularly after discharge. During the five-year follow-up period five had recurrences.

In the two series therefore (bed-rest and U.S.–U.K. Trial) there were 174 patients who did not have recurrences (106 bed rest and 68 U.S.–U.K.) and 24 who did (19 bed rest and 5 U.S.–U.K.).

174 Patients without Recurrences (Table V).—103 had had no or slight carditis in hospital—40 in the U.S.–U.K. trial and 63 in the bed-rest series. Similar numbers in both treatment groups still had slight heart disease at five years, and in none had serious heart lesions developed. Of the other 71 with more marked carditis in hospital (28 U.S.–U.K. trial and 43 bed rest), the cardiac status was also similar in the two groups at five years.

TABLE V.—*Comparison at Follow-up Between Cases Treated with Cortisone, A.C.T.H., or Salicylates, and Bed Rest.* 174 *Patients with No Recurrences*

Cardiac Status in Hospital	No. of Cases	Cardiac Status at Follow-up				
		Normal	Unchanged	Signs Less	Signs More	Died
Carditis nil or slight	103	89	14	0	0	0
U.S.–U.K. trial ..	40	36	4	0	0	0
Bed-rest series ..	63	53	10	0	0	0
Carditis more marked	71	3	50	9	9	0
U.S.–U.K. trial ..	28	1	20	4	3	0
Bed-rest series ..	43	2	30	5	6	0

24 Patients with Recurrences (Table VI).—The recurrence rate was higher in the bed rest series who were not on prophylaxis (15%) than in the U.S.–U.K. Trial who were (6.8%). Four patients in the bed-rest series had more than one recurrence but none in the U.S.–U.K. trial. When last seen for follow-up after the recurrences, none of the five in the U.S.–U.K. trial were worse, whereas in seven of the bed-rest series the signs were more severe and two had died. Six of the nine patients in the bed-rest series who deteriorated or died after the recurrences had had grade 3 murmurs on their first admission here and histories of previous attacks: there were no recurrences in similar cases in the U.S.–U.K. trial.

TABLE VI.—*Comparison at Follow-up of Cases Treated with Cortisone, A.C.T.H., or Salicylate, and Bed Rest.* 24 *Patients with Recurrences*

	Total No. Cases	No. with Recurrences	No. with Increase in Signs	Deaths
Bed-rest series ..	125	19 (15%)	7	2
U.S.–U.K. trial ..	73	5 (6·8%)	0	0

Conclusions.—There was no significant difference in cardiac status at five years between the two treatment groups if those that had recurrences were excluded. With recurrences, on the other hand, patients treated by bed rest alone and no prophylaxis did worse than those in the U.S.–U.K. trial who were given prophylaxis in hospital and after discharge. There were more recurrences in the bed-rest group—sometimes more than one—and many patients were worse or died after them, particularly those admitted with marked carditis in second attacks. In the U.S.–U.K. trial series, on the other hand, recurrences were few; there was never more than one, none occurred in patients admitted with marked carditis in second attacks, and no one was worse after them. We conclude, therefore, that treatment with steroid or salicylate in hospital has little influence on the cardiac status at follow-up, but that prophylaxis, in this case with a sulphonamide, has a beneficial effect by reducing the number of recurrences and thereby preventing further heart damage. Because of this experience, we now institute prophylaxis on patients who were treated in the bed-rest series here and not given prophylaxis in hospital if they are readmitted with recurrences, or as out-patients if they are 16 years of age or less or have had an attack of rheumatic fever within the past five years.

Discussion

There were fewer changes in cardiac status in our series than in those of Ash (1948) and of Bland and Jones (1951), but we followed all our cases for only five years (though some for 6 to 10 years) and they followed theirs for 10 to 20 years. A quarter of Bland and Jones's cases had been discharged with normal hearts and yet had heart disease at 10 years. Similar cases in our own series were all normal at five years, as were the third of them followed for 6 to 10 years. Our experience is therefore that if patients have no heart disease in hospital they will have none at follow-up over periods of 5 to 10 years if there are no recurrences. We also found no serious heart disease in patients who had had grade 1–2 diastolic murmurs as evidence of slight carditis, again excluding those with recurrences. There was therefore nothing to support the view that transitory mitral diastolic murmurs may be the precursors of mitral stenosis, at least up to five years.

Changes in cases with more marked carditis were also slight if there were no recurrences, though in a few the signs became less and in others more. Thus slight mitral or aortic incompetence disappeared in some patients after two to three years, particularly in those admitted in first attacks, and in others aortic incompetence increased or opening snaps developed in addition to mitral systolic murmurs as possible evidence of stenosis; frank stenosis was not observed. Treatment with cortisone, A.C.T.H., or salicylate in hospital did not influence the findings at follow-up, for they were similar at five years whether drugs had been used or the patients treated simply by bed rest.

With recurrences, changes in the heart during the follow-up period were more severe; 30% of the patients who had them became worse or died. Some developed mitral stenosis, which had not been observed in cases without recurrences, and there was close correlation between changes in cardiac status and the total number of attacks: all with frank mitral stenosis had had three or more. This, we realize, is difficult to reconcile with the fact that about 55% of patients with mitral stenosis give no history of rheumatic fever (Parkinson and Hartley, 1946).

Whereas there was no difference at follow-up between the bed-rest and the drug-treated series in those without recurrences, with recurrences there was a marked difference, for half of the series treated with bed-rest became worse or died after them, compared

with none of the U.S.–U.K. series. The bed-rest cases had had no prophylaxis until after this assessment, and the U.S.–U.K. group were given penicillin followed by sulphonamide 1 g. daily in hospital and after discharge. Recurrences were more frequent in the unprotected group: some had more than one, whereas this never occurred in the protected group, and, as has been stated, many unprotected cases were worse after the recurrences whereas there was no deterioration in the protected. The type of case that did worse in the unprotected group, those admitted in second attacks with marked carditis, did not have recurrences while on prophylaxis.

We believe, therefore, that the differences in cardiac status at follow-up between the two groups of cases—one treated with salicylate or hormone in hospital and given prophylaxis and the other by bed rest and no prophylaxis—can be explained wholly by the beneficial effect of prophylaxis in reducing the number of recurrences and thereby the ultimate amount of cardiac damage, and that other drug treatment played no significant part. Thus our finding in the acute phase of the disease—that hormone therapy in the dosage we have used, though of value in special circumstances, does not significantly affect cardiac status in the majority of cases—has been borne out by the subsequent course at follow-up. The results emphasize, however, the value of prophylaxis, and show that this is the most certain method we have at present of reducing morbidity from rheumatic heart disease.

Summary

The follow-up findings over a period of 5 to 10 years in 125 patients with rheumatic fever treated in this unit by bed rest alone and not given prophylaxis are considered separately in 19 who had recurrences and in 106 who did not. Patients without recurrences who had no abnormal heart sign in hospital were normal at follow-up; those with soft (grade 1–2) murmurs were normal or still had soft murmurs (none was worse); with more severe carditis (grade 3 murmurs) there was usually no change at follow-up, but in a few the signs were less (and some returned to normal) and in others more marked (increased aortic incompetence or development of opening snaps in addition to mitral systolic murmurs). With recurrences, however, there was often deterioration and sometimes death, especially in those admitted in second attacks or who had more than one recurrence.

Cardiac status on admission to hospital in these cases and subsequently at follow-up has been related to the total number of attacks of rheumatic fever or chorea. On admission in first attacks, most had no or slight carditis; in second or later ones the majority had marked heart disease. At the last follow-up the majority of those whose cardiac status had deteriorated (including deaths) had had three or more attacks, and mitral stenosis was observed to develop only in such cases.

The findings at follow-up in the bed-rest series, who were not given prophylaxis, have been compared with those in 73 other patients admitted in later years and treated with six-week courses of A.C.T.H., cortisone, or aspirin and given prophylactic sulphonamide 1 g. daily in hospital and after discharge. Nineteen of the bed-rest cases had recurrences but only five of the drug-treated series. In patients without recurrences there was no difference between the two treatment groups in regard to changes in cardiac status at follow-up. With recurrences, on the other hand, there were marked differences: recurrences were more common in the bed-rest series (no prophylaxis) and deterioration was common after them, whereas in the treated (prophylactic sulphonamide 1 g. daily) recurrences were uncommon and no one was worse after them.

It is concluded that treatment in hospital with steroid or salicylate has comparatively little influence in most instances on cardiac status at follow-up, but that prophylaxis has a beneficial effect and is the most certain way we have of reducing the morbidity and mortality rate from rheumatic fever.

My thanks are due to Professor E. G. L. Bywaters for much help and advice in the preparation of this paper.

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PLACE OF RADIOTHERAPY IN TREATMENT OF CANCER OF THE LARYNX*

BY

M. LEDERMAN, M.B., B.S., F.F.R., D.M.R.E.

Deputy Director Radiotherapy Department, Royal Marsden Hospital; Consultant Radiotherapist to Royal National Throat, Nose and Ear Hospital and Metropolitan Ear, Nose and Throat Hospital

There can be no doubt that in the treatment of laryngeal cancer any method that enables the patient to preserve his life and at the same time conserve his larynx must be regarded as the treatment of choice. Radiotherapy alone can do this, and it would seem both humanitarian and in the best traditions of medicine to offer patients this form of treatment wherever possible. It is the purpose of this paper to try to show what radiotherapy can offer sufferers from cancer of the larynx.

Clinical Material

During the period 1933–59 some 959 cases of laryngeal cancer were seen at the Royal Marsden Hospital, and the majority of these (807) were referred without any previous treatment having been given (Table I). Much of the material for this study has been

TABLE I.—*Cases of Cancer of Larynx*, 1933–59

Total number of patients seen		959
Previously untreated cases	807	
Recurrent cases	85	
Post-operative cases	25	
Patients seen but not treated by radiotherapy	42	

drawn from the Royal National Throat, Nose and Ear Hospital, and the Metropolitan Ear, Nose and Throat Hospital. Statistically it is important to emphasize that the patients formed a selected group, since they did not include all the cases seen by all members of the staffs at either the Royal Marsden Hospital or its co-operating hospitals. Some of the cases included in the earlier part of this series were treated by my predecessor, Dr. C. A. P. Wood, and in recent years others have been treated by my colleague, Dr. V. M. Dalley.

*Based upon the Low Beer Memorial Lecture delivered at the University of California on March 3, 1960, and the Leo Rigler Lecture delivered at the University of Minnesota on November 3, 1960.

Classification

The classical division of laryngeal cancer into intrinsic and extrinsic forms (Isambert, 1876; Krishaber, 1879)—a relic of the early days of laryngology—originally served the simple purpose of separating operable from inoperable tumours. It survived for nearly 90 years, which in itself is a tribute to its value; but the advent of radiotherapy, advances in surgery, and, above all, increased knowledge of the natural history of laryngeal cancer, demonstrated quite clearly that it had served its purpose. This fact received international recognition, and recommendations were made for a new classification of laryngeal cancer for international use (Report, 1959).

Three different forms of tumour arising within the larynx have now been identified. Each form behaves in its own special fashion, has its own prognosis, and often requires a different therapeutic approach. The three types of neoplasm are as follows:

1. *Glottic*, arising from the true vocal cord, the anterior or posterior commissures, and forming the commonest and most favourable tumour.

2. *Subglottic*, arising from the subglottic space; these are the rarest tumours, with a much worse prognosis.

3. *Supraglottic*, arising from the ventricular bands, ventricules, or the root of the epiglottis; these are the most serious of the laryngeal tumours, with the worst prognosis.

In this series of 807 previously untreated cases, 559 tumours (70%) were glottic, 174 (21%) supraglottic, and 73 (9%) subglottic in origin; one was not classified.

Staging

In addition to classifying cancer of the larynx according to the site of origin of the neoplasm, some attempt was made to group together individual tumours which resembled each other in their extent—that is, tumours were roughly grouped together according to whether they were early or advanced. This grouping together according to the extent of the tumour is termed "staging," and its main purpose is to provide a reliable basis for assessing prognosis and comparing results obtained by different methods of treatment.

The basis of the system in use at the Royal Marsden Hospital (Lederman, 1952) differs in some respects from the proposed international system. In essence, *Stage I* includes the very early cases where the tumour is limited to its tissue of origin, laryngeal mobility is unaffected, and there are no lymph-node metastases; *Stage II* includes the more advanced tumours where local spread has taken place but the larynx is not fixed and lymph nodes are not present; *Stage III* includes tumours accompanied by fixation of the larynx or homolateral lymph-node metastases, or where extralaryngeal spread has occurred; and *Stage IV* includes the very advanced cancers associated with bilateral or fixed lymph-node deposits or distant metastases.

Fig. 1 shows the distribution of the cases according to stage. The trends over the three periods selected indicate that in the second period (1952–6) the percentage of stage I cases was double that of the previous period, and there was a smaller percentage of advanced stage III or IV cases. In the final period the percentage of cases in stage I remained relatively constant, but there was a significant increase in stage II cases—that is, those most suitable for laryngectomy.

Table II shows the value of the classification in relating the site of the tumour to what is possibly the most important single factor in prognosis of squamous cancer anywhere in the head and neck—namely, the frequency of lymph-node metastases.

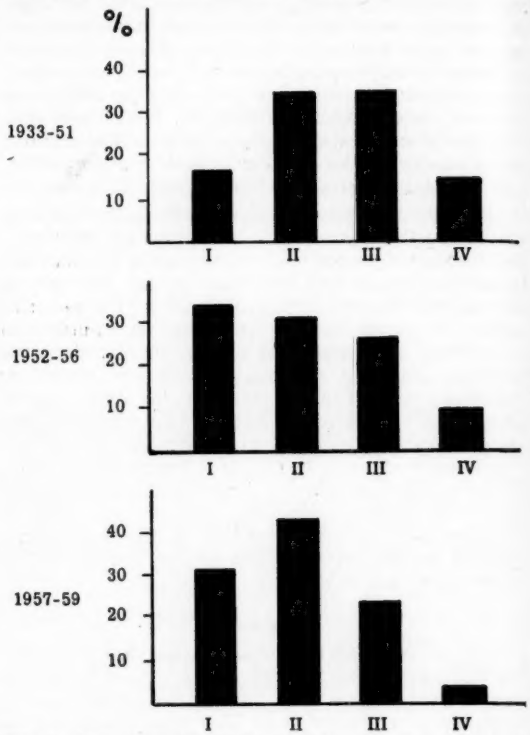

FIG. 1.—New cases treated by radiotherapy. Comparison of stage distribution in three periods.

TABLE II.—*New Cases Treated by Radiotherapy. Incidence of Regional Lymph-node Involvement*

Site of Tumour	Lymph-node Involvement						Total
	−		+		Bilateral		
	No.	%	No.	%	No.	%	
Supraglottic	114	65	60	35	19	11	174
Glottic ..	546	98	13	2	2	0·4	559
Subglottic	66	90	7	10	—		73
Unclassified	1	—	—		—		1
Total ..	727	90·1	80	9·9	21	2·6	807

Cancer of the vocal cord is one of the most "benign" cancers, partly because it tends to be slow-growing, but chiefly because of the low risk of metastases. Lymph-node metastasis is almost unknown where a tumour is strictly limited to the vocal cord; it is only when the tumour has spread from the vocal cord that metastases take place, and then only rarely. By contrast the supraglottic tumours metastasize readily and not infrequently to both sides of the neck (Table II): this difference in behaviour is reflected only too obviously in the treatment results (see Fig. 4).

Age-and-Sex Incidence

Cancer of the larynx is essentially a disease of middle-aged men; only some 7.5% of the patients are women, and the ratio of men to women remained relatively stationary throughout the whole period. It seems to be a curious and unexplained fact that cancer of the head and neck is, with the sole exception of the post-cricoid area, less common and more benign in behaviour

in the female as compared with the male. Table III shows that this may in part be accounted for by the earlier stage at which women seek advice.

TABLE III.—*New Cases Treated by Radiotherapy. Comparison of Male and Female Stage Distribution*

	Stage I		Stage II		Stage III		Stage IV		Total
	No.	%	No.	%	No.	%	No.	%	
Male	198	27	262	35	215	29	64	9	739*
Female	23	34	30	45	11	17	3	4	67
Total	221	28	292	36	226	28	67	8	806*

* 1 unstaged excluded.

Fig. 2 shows that the mean age for both men and women was approximately 61.2 years. The figures remained relatively unchanged over the whole period. The youngest patient was 25 and the oldest 88: both were males. Apart from the peak incidence in the sixth and seventh decades common to both men and women, the latter were proportionately more affected below the age of 40 and above 80.

When considering the age of patients in relation to tumour site, Fig. 3 shows that the supraglottic tumours tended to occur at an earlier and the subglottic tumours at a later age than the common glottic tumours. The subglottic group also showed a rise in incidence below the age of 40 and above 70: this was probably due to the higher incidence of the tumour in the female (Table IV).

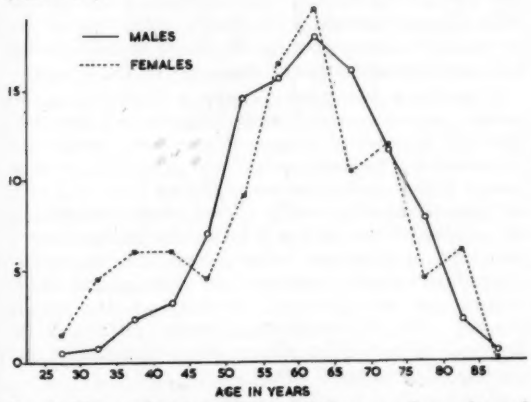

FIG. 2.—New patients treated by radiotherapy. Comparison of proportionate age distributions by sexes.

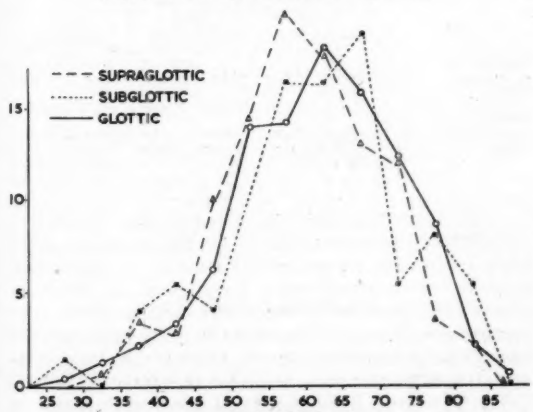

FIG. 3.—New patients treated by radiotherapy. Comparison of proportionate age distributions by site of tumour.

TABLE IV.—*Site Distribution in Relation to Sex*

	Male	Female	Total
Supraglottic ..	161	13	174
Glottic	516	43	559
Subglottic ..	63	10	73
Unclassified ..	—	1	1
Total ..	740	67	807

Predisposing Factors

Syphilis.—Routine serological tests for syphilis were abandoned at the outbreak of the last war and have not been resumed. There is no reason to believe that this disease has any significant relationship to the causation of laryngeal cancer.

Smoking.—Our records in relation to the smoking habits of patients were incomplete, since in the early years covered by this report the possible relationship between cancer of the respiratory tract and tobacco was not appreciated, and so our records covered only the more recent years after this possibility had come to the fore. We can only offer a negative observation—namely, that it is most unusual to encounter laryngeal cancer, particularly vocal-cord cancer, in the non-smoking male. Such few non-smokers as were seen were mostly women suffering from subglottic cancer.

Vocal Abuse.—Among our patients there were many whose livelihood depended on their voice—that is, parsons, actors, singers—but again there is no evidence to show that these people are more likely to develop laryngeal cancer than those in other occupations where use of the voice is not so dominant.

Pre-malignant Lesions (Lederman, 1961).—A previous history of papilloma, leucoplakia, or keratosis was occasionally encountered: because our material was selected and the patients with these lesions were referred for treatment after the development of malignancy it was impossible to determine the frequency with which this change occurred. Premalignant lesions were not treated by radiotherapy for the following reasons. (1) There was no certainty that malignancy would supervene in any given case, and, even if it should, the time interval might be very long. (2) Pre-malignant lesions are not particularly radiosensitive and full doses of radiation would have had to be given with all its attendant discomforts and risks (Report, 1959). There was, moreover, no guarantee that even when apparently successfully treated by radiation recurrence might not later take place and malignancy then supervene, in which event the patient would be worse off, since in these circumstances he would be debarred from further use of radiation at a time when he might most need it.

Treatment Policy

Since early laryngeal cancer can be treated successfully by both radiotherapy and surgery, these are to be regarded as competitive methods. The advantages of radiotherapy are, however, so overwhelming that they cannot, or should not, be ignored. These particular advantages are: (1) avoidance of an operation, (2) preservation of a normal voice, and (3) the patient is given two chances of survival. If the patient submits to surgery first and recurrence takes place, the radiotherapist can do very little for him, since the post-operative irradiation of cancer cells in scar tissue is rarely of value.

In this series all early cases in stage I and II—that is, those without laryngeal fixation and unaccompanied by lymph-node metastases—received radiotherapy without any equivocation. The presence of some associated pre-malignant condition such as leucoplakia or keratosis may add to the technical difficulties of treatment and reduce the prognosis with radiotherapy, but these complicating conditions should not be regarded as an excuse for advocating surgery in preference to radiotherapy, since the latter may still prove successful and the patient's larynx thereby be spared.

For the advanced case there should be little competition between the surgeon and the radiotherapist. Surgery is certainly the mainstay of treatment for the following cases: (1) stage III and IV cases, particularly when complicated by laryngeal fixation, lymph-node metastases, or perichondritis; and (2) for recurrent cases after previous conservative surgery or radiotherapy.

The prognosis by any method of treatment for these advanced cases is not very good and we believe a preliminary course of radiation to be of value. The chief advantages of this combination are: (1) a small number of tumours, particularly in stage III, proved radiosensitive and the need for operation did not arise (see Fig. 9); (2) a preliminary course of radiotherapy caused the growth to shrink and could bring a doubtfully operable tumour into the bounds of operability; (3) it enabled the extent of an operation to be reduced—for example, if a pharyngeal extension regressed under radiotherapy the subsequent operation could be limited to laryngectomy instead of pharyngolaryngectomy; and (4) the incidence of recurrences in the tracheostome, particularly in the subglottic group, could be reduced by preliminary irradiation of the whole of the cervical trachea.

Extensive inoperable tumours, particularly in elderly patients, were treated by palliative radiotherapy alone; but the advanced age of the patients was never used as an argument against the routine employment of radiotherapy if the tumour was early.

A six-weeks period was allowed to elapse between the end of the treatment and the assessment of its success or failure. If at the end of this period the larynx was normal the patient was followed up regularly; if the larynx had not returned to normal and there was persistent ulceration, residual infiltration, or fixation, then a direct examination was performed and a biopsy specimen taken only from a frankly tumorous or suspicious area. If, on direct examination, the mucosa was found to be intact and there was no suspicious area, biopsy was not performed, since this procedure might, by destroying the integrity of the mucous membrane, facilitate infection and provoke perichondritis. If the biopsy was positive laryngectomy was performed with the minimum of delay.

In the more advanced cases it was sometimes difficult to reach a definite decision since the larynx might look suspicious, and ulceration, fixation, and oedema might be present, but biopsy might be repeatedly negative. We believe it is justifiable in these cases to advise laryngectomy, as, in our experience, advanced cases which do not present a reasonably normal appearance after radiotherapy are rarely cured; to await a positive biopsy very often means waiting too long and the patient could forfeit his chance of cure by surgery. Where laryngectomy has been performed in these circumstances it is rare not to find cancer cells in the operative specimen. The timing of the surgery in relation to the radiotherapy was important. The interval of six weeks after the termination of treatment was chosen, partly because at the end of this time it could be assumed that the maximum tumour regression in response to the radiation had occurred; and, more important still, if the treatment failed there was less chance that during a laryngectomy performed between 6 and 12 weeks after radiation tissue fibrosis, troublesome bleeding, and delayed healing would be encountered to the same extent as would have been the case if the operation was performed after the third month when the post-radiation changes likely to cause these difficulties had become firmly established (Mill, 1956; Ormerod and Shaw, 1956).

Preparation and Care of the Patient

Patients in good general condition with early carcinomas required little preparatory treatment. A routine blood count and radiographic examination of the larynx and chest were undertaken. A Wassermann test was done only if there was a history of syphilitic infection or clinical features suggested that possibility.

The routine radiographic procedures were thought to be of prime importance, since soft-tissue radiography (lateral view and tomography) provided a great deal of information that could not be obtained by purely clinical or instrumental measures. The routine examination of the chest was also performed to exclude pulmonary tuberculosis, to detect other pulmonary infectious complications, and to ensure that the patient had not a further primary neoplasm of the bronchus.

A preliminary biopsy was routinely performed except where a patient had such severe respiratory obstruction that the trauma of biopsy might have precipitated tracheotomy. Occasionally in the very frail or senile patient this procedure was not insisted upon. It is of the utmost importance that a preliminary tracheotomy be avoided if the patient is to receive benefit from a course of radiotherapy. The patient with respiratory obstruction unless *in extremis* was given prompt radiotherapy and by this means tracheotomy was usually avoided. Once a tracheotomy was performed the technique of treatment became more complicated and the prognosis worse (Table V).

TABLE V.—*Tracheotomy in Relation to Radiotherapy. Fifty-two Operations*

Site	Before Radiotherapy	During Radiotherapy	After Radiotherapy
Supraglottic	3	4	7
Survival	None at 5 years	None at 5 years	None at 5 years
Glottic	12	3	15
Survival	2 at 5 years	None at 5 years	3 at 5 years
Subglottic	6	1	1
Survival	None at 5 years	None at 5 years	None at 5 years
Stage	All cases Stage III or IV	All cases Stage III	21 cases Stage III and IV, 1 Stage I, 1 Stage II

Apart from the cases where biopsy was omitted, it occasionally happened that a biopsy specimen, even when taken, was subsequently found to be inadequate, negative, or unsatisfactory. An attempt was made to repeat this operation if there was clinical doubt concerning the diagnosis, but where no such doubt existed and if the patient had already started radiation treatment it was thought to be unwise to repeat the procedure. Table VI shows the different histological varieties of tumour encountered and also the number of patients for whom no histological confirmation of the diagnosis

TABLE VI.—*Previously Untreated Patients Treated by Radiotherapy (1933–59) Classified According to Histology*

Squamous-cell carcinoma and carcinoma not otherwise specified	608
Carcinoma specified as poorly differentiated, undifferentiated, or anaplastic	77
Carcinoma *in situ*	66
Adenocarcinoma	1
Unconfirmed	52
Other malignant tumours	3
	807

was available: the accuracy of the clinical diagnosis was, however, borne out by the results, since most of them died of cancer (see Fig. 7).

The problem of the teeth required consideration, and septic teeth were removed even when not within the field of radiation. The smoking and drinking habits of the patient were not curtailed to such an extent that he was made miserable. He was advised to give up smoking, but, if he did not wish to do so, smoking was restricted to the postprandial cigarette, pipe, or cigar. Equally, drinking habits were controlled; alcohol in the form of spirits was forbidden, but beer or wine was permitted. Fit patients who lived near the treatment centre were not admitted to hospital and most of them had treatment as out-patients, though some required admission for the terminal part. The attitude towards working depended upon the patient's temperament and job. In principle, we found that the patient was a happier and more contented person the less his normal routine life was disrupted. The following people, however, were admitted to hospital: the elderly, the debilitated or sick patients, those with advanced disease, and those living far from the treatment centre.

Patients with tuberculosis or other respiratory diseases tolerated radiation well but were usually admitted, and those presenting with stridor or respiratory obstruction were always admitted as emergencies. If, as should be the case, the patient's larynx was to be examined very often during radiation treatment, the difficult subject was taught how to "show his larynx." It was most exceptional to find individuals who did not respond to patient and correct instruction. Resort to regular cocainization was practically never necessary.

Technique of Treatment

The technique of treatment depended on the age, general condition of the patient, and the site, histology, and extent of the tumour. A haemoglobin of 60% was regarded as the lowest limit for radiotherapy: below this level a blood transfusion was given.

All early cases of laryngeal cancer were treated by telecurie therapy and we had at our disposal a variety of specially designed head and neck units containing radium, cobalt, and, more recently, radioactive caesium. *X*-ray therapy at conventional voltages was reserved for the palliative treatment of advanced or recurrent cases. In telecurie therapy a protracted fractionated system of dosage was used: a dose of 300 r a day was given to one or two fields for five or six days a week, the total tumour dose varying from 5,500 to 8,000 r in six to eight weeks.

Post-radiation Complications and Sequelae

Under modern conditions with present-day equipment technique and knowledge of dosage, post-radiation complications should rarely be encountered and severe damage such as radio-necrosis never at all.

There were four main post-radiation complications that haunted the radiotherapist in the past: (1) laryngeal oedema, often severe enough to require tracheotomy; (2) perichondritis; (3) cartilage necrosis; and (4) changes in the irradiated skin. In this series of patients these complications were prevented by attention to the following factors.

Selection of Case.—The advanced cases of cancer of the larynx were always associated with malignant perichondritis and most of these patients ultimately required surgery. If preliminary radiotherapy was decided upon, then, bearing in mind that its purpose was largely pre-operative rather than curative, the daily dose, the overall treatment time, and dosage were selected so as not to aggravate the already existing perichondritis. The use of antibiotics helped considerably in cases of this kind. If the perichondritis could not be controlled there was little point in persevering with radiotherapy, and if the lesion was operable the patient was submitted to operation without delay.

Selection of Apparatus.—Gamma-radiation was considered preferable to conventional 200-kV *x*-radiation.

Control of Radiation Reactions.—Radiation treatment had to be adapted to the patient and his tumour. This could be achieved by attention to daily and overall dosage and the total time over which the treatment was spread. Extending treatment over a minimum period of six weeks resulted in a comfortable patient and generally the patient who did not suffer during treatment rarely encountered complications after treatment.

Among the patients in this study the incidence of post-radiation complications was very small. Tracheotomy for radiation oedema during treatment was almost unknown, and if it did become necessary it was nearly always regarded as being the fault of the radiotherapist. Post-radiation tracheotomy, with very rare exception, was due to failure to control the disease. There were only two cases of skin necrosis in this whole series, and for the past 10 years the skin changes during radiation therapy were restricted to a mild dry desquamation, and post-radiation subcutaneous fibrosis or telangiectasis was not encountered. Persistent localized laryngeal oedema were occasionally seen when high dosage had to be given, and were found particularly among the supraglottic group of tumours. A mild perichondritis as evidenced by localized tenderness and oedema of the larynx and homolateral earache was also occasionally encountered, usually after a history of respiratory infection. It responded well to voice-rest and treatment by antibiotics. Necrosis of the endolaryngeal soft tissues was extremely rare.

Results of Treatment

In dealing with a disease such as cancer, for which no certain remedy exists, it is easy to become a partisan of a particular method of treatment. In order to avoid this very human weakness statements concerning treatment policy must be based upon the evidence provided by treatment results. Radiation techniques or surgical operations designed for the curative treatment of malignant disease do not merit serious consideration unless they are supported by results. Figs. 4–7 show the results achieved by our policy of irradiation as the method of choice with surgery reserved for failures.

All results reported here are quoted as crude survival rates. Patients who were lost to follow-up and those who died from intercurrent disease were counted as died of cancer. As many of our patients were elderly and many came from foreign countries where the importance

of follow-up is seldom appreciated, these cases represented a serious statistical liability.

There was a further loading against radiotherapy because of the epoch covered by this report—namely, the pre-laryngectomy and pre-antibiotic era, when the Royal Cancer Hospital, as it was then known, was almost a home for the dying and patients were admitted moribund and given perhaps one or two radiation treatments before expiring: yet these patients, nevertheless, were included.

The influence of site, stage, and sex is shown in Figs. 4, 5, and 6. The significantly better results in women are well shown, as is also the marked influence of stage upon results. So long as the larynx remained mobile and lymph nodes were absent, the prognosis was very good even at 10 years. The advanced cancers in stage III and IV were cured in only a minority of cases whatever was done. Although it was exceptional to see any tumour other than an epithelioma, the differences in results at five years between the differentiated and undifferentiated epitheliomata were noteworthy (Fig. 7). The excellent prognosis of patients with "carcinoma *in situ*" is well shown.

Figs. 4–7 give the results obtained without reference to the precise method of treatment. Table VII, based on the stage of the disease, illustrates the part that laryngectomy plays in relation to radiotherapy. Some 70% of the patients, whose radiation treatment was unsuccessful, came to surgery within the first year after treatment: only a very small proportion (4%) of patients required laryngectomy for recurrence after the third year. The need for laryngectomy was least in stage I (13.6%) and highest in stage III (34.5%). Only a minority of stage IV cases ever merited the attempt at laryngectomy.

Some 22% of all patients treated had to undergo post-radiation laryngectomy: in approximately a similar percentage of the survivors after three and five years the

TABLE VII.—*Laryngectomy after Radiotherapy* (1933–56)

Stage	Total No. of Cases	Total No. Undergoing Operation	Time Elapsing	
			Within 1 Year of Radiotherapy	After 3 Years
I	139	19 (13·6%)	11	2
II	181	37 (20·4%)	23	2
III	165	57 (34·5%)	44	1
IV	61	10 (18%)	9	—
	546	123 (22·5%)	87 (70·7%)	5 (4%)

Of these 546 patients, 326 (60%) survived three years: 68 (21·5%) after laryngectomy. At five years 190 (48%) of 395 patients survived: 44 (23·1%) after laryngectomy.

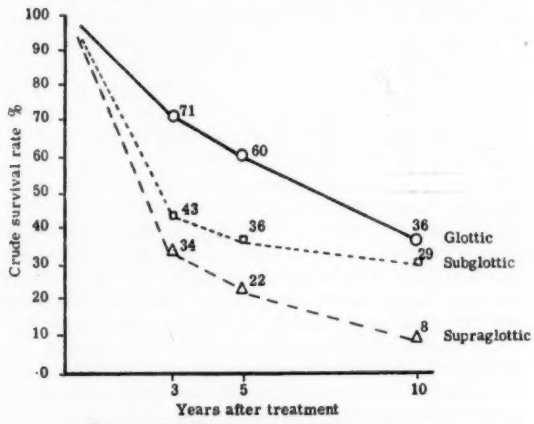

FIG. 4.—Results according to site of tumour.

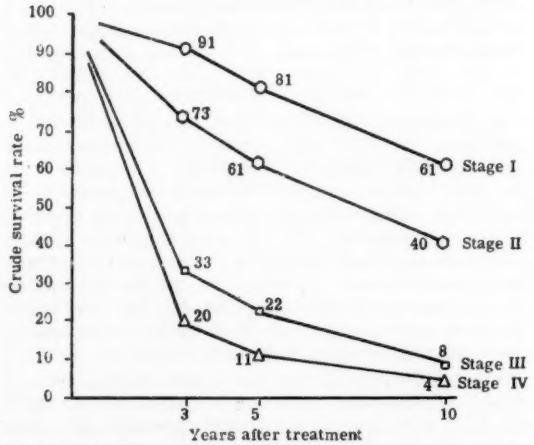

FIG. 5.—New cases treated by radiotherapy. Results according to stage.

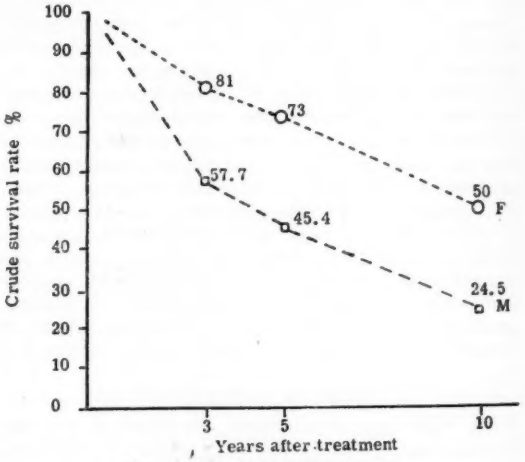

FIG. 6.—Results according to sex.

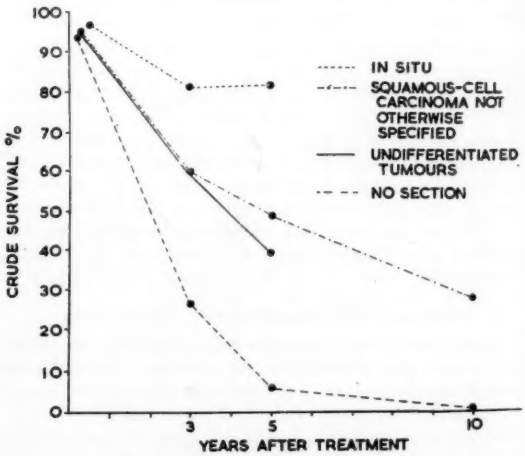

FIG. 7.—Results according to histology.

larynx had to be sacrificed. The outstanding achievement of radiotherapy lay in the fact that nearly four-fifths of the survivors retained the larynx.

Fig. 8 shows the results in relation to site and laryngectomy. Again it can be seen that the majority of survivors retained the larynx whatever the site of origin of the tumour, and in this connexion the results obtained in the subglottic group are of interest. This is the rarest of the laryngeal tumours and the one to which the surgeon lays claim on the alleged grounds that they are insensitive to radiation. From the results shown in Fig. 8 there is no doubt that some subglottic carcinomas were curable by radiotherapy, and they were generally the tumours in women, situated in the anterior half of the subglottic space, the vocal cords remaining mobile and nodes being absent.

Supraglottic cancers are the most deadly of the laryngeal cancers, chiefly because of the lymph-node problem, but also because they are situated in a part of the larynx where the pre-epiglottic space and the laryngeal cartilages are most readily invaded. Radiotherapy was the main hope for these patients, with surgery very much in the background.

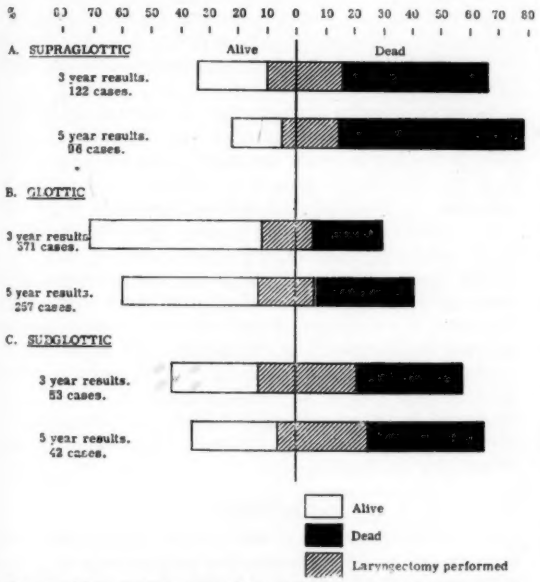

FIG. 8.—New patients treated by radiotherapy. Three-year crude survival rates (1933–56) and five-year crude survival rates (1933–54) by site, showing the number of patients requiring laryngectomy after radiotherapy.

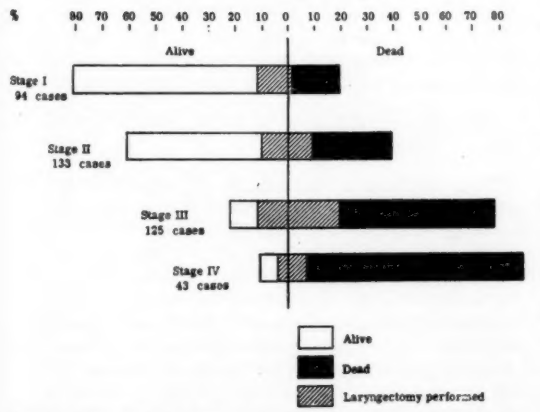

FIG. 9.—New patients treated by radiotherapy. Five-year crude survival rates (1933–54) by stage, showing the number of patients requiring laryngectomy after radiotherapy.

Fig. 9 shows the results in relation to stage and laryngectomy. In stages I and II only a small proportion of the survivors had to sacrifice the larynx, whereas in stages III and IV the survivors were few and approximately half owed their survival to laryngectomy.

Conclusions

All cases of early or moderately advanced laryngeal cancer ordinarily regarded as suitable for laryngo-fissure or laryngectomy should be treated by radiotherapy for preference, since the results obtained by this method are good and the functional result is as a rule excellent.

Radiotherapy is only occasionally successful in the treatment of advanced cases of laryngeal cancer, and surgery must be regarded as the mainstay of treatment. Until such time as more statistical information is forthcoming concerning the value of surgery alone for this group of cases, a preliminary course of radiotherapy has much to commend it.

Incomplete operations for advanced laryngeal cancer are inexcusable, and to send such patients to the radiotherapist in the hope that post-operative radiotherapy will succeed where surgery has failed betokens a faith in radiotherapy that cannot be justified.

Some subglottic cancers can be cured by radiotherapy: and those that cannot may yet benefit from pre-operative irradiation, since the risk of recurrence in the tracheostome may be reduced.

The supraglottic lesions are the most serious of laryngeal cancers. The early cases can be cured by radiotherapy alone, but the advanced cases with lymph-node metastases are only exceptionally cured by any combination of methods.

In the series of cases reported here, approximately one in five of the patients required laryngectomy after radiotherapy; of the patients surviving three and five years, four out of five retained the larynx.

Summary

During the period 1933–59 a total of 959 cases of laryngeal cancer were seen at the Royal Marsden Hospital, 807 being previously untreated. The primary tumour was glottic in 70% of the cases, supraglottic in 21%, and subglottic in 9%. The average age of the patients was 61.2 years, and 7.5% were women. No special predisposing cause was apparent, although it is unusual to see laryngeal cancer in non-smokers.

The treatment adopted was telecurietherapy, using gamma radiation from a radium and more recently from a cobalt source. *X*-ray therapy was employed only for palliation. Surgery was reserved for radiation recurrences or failures, the success or failure of treatment being assessed within six weeks of its termination. Post-radiation damage was rarely encountered, nor was any subsequent surgery hampered by the preceding radiotherapy.

The three-year and five-year survival rates for all patients was 60% and 48% respectively; among the former 21.5% of the patients had undergone laryngectomy after radiotherapy, and among the latter 23.1%.

I am indebted to my colleagues at the Royal Marsden Hospital and its co-operating hospitals for referring the patients. I thank Dr. Robert S. Stone and Dr. Franz Buschke, of the radiation therapy department of the University of California Hospital, San Francisco, and Dr. Donn Mosser, director of the radiation therapy department of the University of Minnesota Hospital, Minneapolis, for permission to draw upon material used for the first Low Beer Memorial Lecture and the fifteenth Leo Rigler Lecture respectively. Dr. Henry Stratton, of Messrs. Grune and Stratton, has kindly given me permission to use material which has been already incorporated in my forthcoming book on cancer of the larynx and laryngopharynx. Finally, I wish to thank my secretary, Miss Morehead, for the preparation of the manuscript, and Mr. Payne, statistician to the Royal Marsden Hospital, for providing the tables and figures.

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INCIDENCE AND AETIOLOGY OF THYROID CARCINOMA

BY

J. WILLIS, M.D.

Department of Pathology, Queen's University of Belfast

The reported incidence of thyroid carcinoma, even when calculated on material gleaned from similar populations, shows marked discrepancies and has given rise to widely contrasting opinions regarding its importance as a cause of death. Likewise, opinions differ on the incidence of malignant change in surgical material, particularly when consideration is given to non-toxic nodular goitre. This is due to the fact that such figures depend upon the policy of the surgeon, the type of centre from which they are reported, and the histological criteria used in the diagnosis of malignancy.

Furthermore, during the past decade the potential carcinogenic effects of the therapeutic use of irradiation to the cervical region and of antithyroid drugs for benign thyroid states has often been a matter of speculation.

Northern Ireland, with a relatively stable population and readily accessible material, was regarded as ideal for a study of the incidence and possible aetiological factors of thyroid carcinoma in man because it is possible to include all surgical cases from both urban and rural hospitals, thus avoiding the selective factor which influences reports from centres specializing in thyroid disease.

Material

Most of the material (Table I) used in this study includes those cases in which the diagnosis was made by histological examination over a 25-year period (1934–58) in the department of pathology, the Queen's University of Belfast, and a four-year period (1955–8) in the laboratories of Belfast City Hospital. Special reference is made in the text when additional cases are included. All surgical specimens from the whole of Northern Ireland are submitted to one or other of these two departments.

TABLE I.—*Source, Period of Observation, and Pathological Diagnosis of Surgical Thyroid Specimens*

	University Department (1934–58)	Laboratories, B.C.H. (1955–8)
Non-toxic solitary nodular goitres	658	173
,, multiple ,, ,,	*728*	*211*
Total non-toxic nodular goitres	1,386	384
Primary hyperthyroidism	899	219
Secondary ,,	178	39
Primary carcinoma	122	27
Hashimoto's disease	49	12
Miscellaneous	252	23
Total	2,886	704

In all cases representative sections were available for review. The criteria of malignancy used in this study are the same as those generally applied to cancer of all other organs. These include changes in cell type and staining reactions, aberrant nuclear forms and hyperchromatism, increased mitotic activity, loss of organoid pattern, capsular, lymphatic, or venous invasion, and finally metastases.

However, in some tumours the morphological changes were thought to be insufficient and the diagnosis of malignant change could be made with certainty only by demonstrating invasion or metastases. Such tumours included encapsulated and well-differentiated ones and those removed from patients who had received antithyroid therapy prior to operation.

The information concerning the use of irradiation and antithyroid drugs for thyroid disease before the diagnosis of malignant change was collected either by personal interrogation of the patients or indirectly by a questionary sent to consultants and general practitioners who had at any time seen the patients. That regarding a history of thyrotoxicosis was obtained by an examination of the case-notes recorded by the physicians or surgeons.

Incidence

Necropsy Material.—In this study thyroid cancer was encountered on 15 occasions in 15,100 necropsies. This incidence of 0.1% agrees with that reported by Wilson (1921) for the United States, Zimmerman *et al.* (1950), and Steiner (1950), but differs from that recorded by Vanderlaan (1947), who could find only five cases of thyroid malignancy in 18,668 necropsies.

Registrar-General's Records. — The figures for Northern Ireland are shown in Table II. During a three-year period (1955–7 inclusive) the cause of death was attributed to carcinoma of the thyroid gland in 14, 16, and 11 cases respectively. Taking the average figure for the three years, thyroid cancer accounted for 0.6% of all cancer deaths.

TABLE II.—*Statistics Reported by the Registrar-General for Northern Ireland*

	1955	1956	1957	Average
Total deaths due to all types of cancer	2,170	2,201	2,306	2,228
Deaths due to thyroid cancer	14	16	11	14
Percentage of all cancer deaths due to thyroid cancer	0·6	0·7	0·5	0·6

Surgical Material.—The frequency with which thyroid cancer occurs in surgical material is shown in Table III.

TABLE III.—*Incidence of Primary Carcinoma in Surgical Thyroid Specimens*

Type of Goitre	No. of Surgical Specimens	No. of Carcinomata	Percentage Carcinomata
Whole series	3,590	149	4·1
Non-toxic nodular	1,900	130	6·8
,, solitary nodular	925	94	10·2
,, multinodular	975	36	3·7
Hashimoto's disease	63	2	3·2
Toxic	1,348	13	1·0
Miscellaneous	279	4	1·4

The overall incidence of 4.1% is comparable to those reported by Crile and Dempsey (1949), Cattell and Colcock (1953), Majarakis *et al.* (1953), Ross (1956), and Shallow *et al.* (1956).

That malignant change is more often associated with non-toxic nodular goitre (6.8%) than with toxic nodular goitre (2.3%) has been well documented by Cole *et al.* (1949), Beahrs *et al.* (1951), and Majarakis *et al.* (1953). At variance with this finding is the report by Sokal (1954), who calculated that malignant change was more common in toxic nodular goitre.

When the non-toxic nodular group is broken down into solitary nodular and multinodular types, it is seen that the incidence of carcinoma is significantly higher in operated solitary nodular goitre (10.2%) than in multinodular (3.7%). A similar experience has been recorded by Cope *et al.* (1949), Crile and Dempsey (1949), Cole *et al.* (1949), Majarakis *et al.* (1953), and Crabtree and Hunter (1953). On the other hand, Friedell (1941), Fisher and Fisher (1951), and Martin (1954) found a higher incidence of malignancy in multinodular goitre.

It is well recognized that carcinoma rarely develops in the presence of toxic diffuse goitres; Means (1937) remarked that thyrotoxicosis appeared to be an assurance against the development of thyroid carcinoma. However, associated toxicity may reduce but does not exclude the possibility of malignancy. In this series, 13 patients have unequivocal evidence of toxicity which includes primary and secondary thyrotoxicosis. Thus 8.7% of patients with thyroid cancer exhibit evidence of toxicity or 1% of patients with thyrotoxicosis have a primary carcinoma of the thyroid gland.

The reported incidence of toxicity in malignant goitres varies from none in 256 cases (Levitt, 1954) to 26% in 112 cases (Ward *et al.*, 1950). Again, the incidence of malignancy in primary thyrotoxic goitres varies from 0 (Herbst, 1924) to 0.8% (Cope *et al.*, 1949). The discrepancies are no doubt due to the small number of cases in some series and to the lack of uniformity of the criteria used in the diagnosis of thyrotoxicosis as pointed out by Kilpatrick *et al.* (1957) and Jude *et al.* (1958).

Changing Incidence of Thyroid Carcinoma.—The increasing frequency with which carcinoma is being diagnosed in the thyroid gland has been commented on by Horn and Dull (1954), Shallow *et al.* (1956), Greene (1957), and Hershey (1958). This study proves no exception. Considering the surgical material submitted to the university department, it is seen from Table IV that 11 cases were diagnosed between 1934 and 1938 inclusive, and 57 cases between 1954 and 1958 inclusive. The increase is due to the equivalent increase in the number of operations for nodular goitre, which is known to harbour carcinoma and to the increase in the number of operations. Other factors which must be considered in the reported increase are the earlier recognition of carcinomatous changes by pathologists and the changing pattern in histological types which has been observed by Beahrs *et al.* (1951) and by Crile (1953).

The relationship between the therapeutic use of antithyroid drugs and radiation for benign thyroid states and the present increase in carcinoma of the thyroid gland is discussed below.

TABLE IV.—*Change in Frequency of Diagnosis of Certain Conditions Found in Surgical Thyroid Specimens*

	1934–8	1954–8	Approximate Increase
No. of carcinomata	11	57	×5
,, ,, nodular goitres	104	507	×5
,, with primary thyrotoxicosis	84	310	×4
Miscellaneous	51	90	×2
Total No. of operations	250	964	×4

Antithyroid Drugs and Thyroid Carcinoma

Seventy-three of the patients with carcinoma of the thyroid gland who were diagnosed in Northern Ireland between January 1, 1946, and February 28, 1959, have been interrogated regarding therapy with antithyroid drugs before the diagnosis of malignancy. A positive answer has been noted in four cases. In two of these there is also a history of previous *x*-ray therapy to the thyroid gland for thyrotoxicosis, and so the details are described in the next section. The clinical features of the two remaining cases are as follows.

Case 1.—A woman aged 29 was admitted to hospital in May, 1956, for the investigation of persistent diarrhoea. Primary thyrotoxicosis was correctly diagnosed, and treatment was started with carbimazole 10 mg. three times daily, which was reduced to 5 mg. three times daily in September, 1956. The drug was stopped in January, 1957, because it was not giving the desired effect. In November, 1957, malignant change in the thyroid gland with metastases in the cervical lymph nodes and lungs was suspected; this was confirmed at operation, when most of the main mass of tumour involving the right lobe of the thyroid with extensions into the thoracic inlet and lymph nodes was excised. Histological examination revealed a primary sclerosing carcinoma of the thyroid gland with metastases in the regional lymph nodes. The duration of the carbimazole therapy was seven months.

Case 2.—A woman aged 30 was admitted to hospital in June, 1957, when a diagnosis of primary thyrotoxicosis was made. Carbimazole 5 mg. three times daily was given, increased four months later to 10 mg. three times daily, with a further increase nine months later to 10 mg. four times daily. This was reduced after seven weeks to 10 mg. three times daily and subsequently to 5 mg. three times daily in January, 1959. The drug was discontinued in February, 1959, three weeks before partial thyroidectomy was carried out. Histological examination revealed diffuse hyperplasia with a clear-cell carcinoma of the thyroid gland 1 cm. in diameter. The duration of carbimazole therapy was 19 months.

Irradiation and Thyroid Carcinoma

Eighty-one of the patients with thyroid carcinoma have been interrogated for a history of exposure of the thyroid gland to irradiation. The remaining patients are either dead or attempts to trace them have been unrewarding. In five cases an affirmative answer has been received. The clinical details of three of these cases, with reference to a fourth case, have been reported (Willis, 1959). However, the reported data of Case 3 did not include the dose and duration of the carbimazole

therapy and so they are repeated in this paper. The fifth case is also reported. Unfortunately the dose of irradiation is not known.

Case 3.—A woman aged 46 who had had *x*-ray therapy in 1937 for thyrotoxicosis at the age of 26, was admitted to hospital in July, 1957, in congestive heart failure complicating thyrotoxicosis, which settled down with carbimazole and digoxin therapy. The carbimazole, 15 mg. three times daily, was started shortly after admission and reduced to 10 mg. three times daily two weeks later, with a further reduction to 5 mg. three times daily six weeks after. The drug was discontinued in February, 1958, when a partial thyroidectomy was carried out. Examination revealed a papillary carcinoma in a diffusely enlarged thyroid gland. The duration of the carbimazole administration was seven months, and the latent interval between the time of irradiation and diagnosis was 21 years.

Case 4.—A woman aged 27 attended hospital in 1943, when a diagnosis of thyrotoxicosis was made; subsequently she was treated by *x*-ray therapy. This resulted in an amelioration of the symptoms until June, 1945, when there was a recrudescence of her thyrotoxic state; thiouracil 200 mg. daily was prescribed, but was soon reduced to 100 mg. daily, which was continued for five months. The drug seemed to have little success, so that the patient took it only spasmodically until her readmission to hospital in 1947, when regular therapy with thiouracil was reinstituted and continued without complete control of symptoms until October, 1950, when partial thyroidectomy was carried out. The patient remained well until 1955, when she had a recurrence. Again thiouracil 100 mg. daily was prescribed, but it was changed to carbimazole 5 mg. twice daily in 1957; this was discontinued in November, 1958, but was restarted a few weeks later and continued pre-operatively for two weeks in a dose of 15 mg. three times daily.

Examination of the partial thyroidectomy specimen revealed a papillary carcinoma in a very nodular thyroid gland. The duration of carbimazole therapy was nine years and the latent interval between time of irradiation and diagnosis was 15 years.

Discussion

The relatively low incidence of carcinoma of the thyroid gland in necropsy material in contrast to the frequency with which the diagnosis is made in surgical specimens has formed the subject of discussion for many writers (Vanderlaan, 1947; Rogers *et al.*, 1947; Sokal, 1953). In the present study the diagnosis of thyroid cancer was made in the university department by histological examination of surgical specimens from 122 patients during the 25-year period 1934 to 1958 inclusive. Necropsy examination was available on only 15 cases.

It seems reasonable, in such a condition as thyroid cancer, to accept the Registrar-General's figures as a true indication of the occurrence of this disease as a cause of death. Thus the fact that carcinoma of the thyroid was encountered eight times more often in surgical than in necropsy material cannot be explained on the basis of misdiagnosis by pathologists of benign lesions as cancer, which was implied by Vanderlaan (1947) and Astwood (1956), because the number of deaths from this condition registered in Northern Ireland is comparable to the number of cases diagnosed in this way. For example, during a three-year period 1955 to 1957 inclusive, the number of deaths due to thyroid cancer according to the Registrar-General for Northern Ireland was approximately 14 a year, while the number of cases diagnosed on surgical material was 17 a year.

The discrepancy in the figures quoted can be explained by the increasing frequency with which thyroid cancer is being diagnosed in surgical material, so that the number dying in any one year will be less than the number diagnosed in the same year. Furthermore, there are some localized tumours diagnosed by histological examination of the surgical specimens, particularly in diffuse toxic goitres but also in non-toxic goitres, which are compatible with longevity. However, some of the patients succumb from other diseases, and the fact that they had thyroid cancer may not be notified to the Registrar-General.

Thus the paucity of cases with thyroid cancer coming to necropsy is due to the fact that in the majority of fatal cases either the patients die at home or permission for necropsy is not granted. This aspect of the problem has previously been emphasized (Anglem and Bradford, 1948; Cole *et al.*, 1949; Dailey *et al.*, 1950).

The possibility that antithyroid drugs might be carcinogenic in man has often been speculated on (Hinton and Lord, 1945; Lerman *et al.*, 1946; Taylor, 1947; Cope, 1952; Levitt, 1954). In the present study, 4 of the 73 patients interrogated gave a history of antithyroid therapy prior to the diagnosis of malignant change in the thyroid gland. In two cases carbimazole had been prescribed for 7 and 19 months respectively. Experimentally it requires the administration of antithyroid drugs for approximately half the life-span of the rat before malignant tumours occur (Purves and Griesbach, 1947; Willis, 1959, unpublished). Although the results of animal experiments are not always applicable to man, the duration of therapy in both cases is thought too short to have had any significant carcinogenic effect, but it cannot be completely exonerated in the latter case.

The remaining two cases had taken the antithyroid drugs for 7 months and 9 years respectively, but in addition they had received irradiation 21 and 15 years respectively before the diagnosis of thyroid cancer. In the former case the duration of medical therapy is once again thought to be too short, while in the fourth case the antithyroid drugs can neither be accused of nor exonerated from having induced the malignant change because of the potential carcinogenic effects of the *x*-ray therapy. However, the subsequent administration of the antithyroid drugs might have hastened the onset of malignancy, which is known to occur in animals (Doniach, 1953). The results of this investigation indicate that the therapeutic use of antithyroid drugs is not the full explanation for the increasing incidence of thyroid cancer in this country over the past decade.

Although thiouracil has been widely used since its introduction by Astwood in 1943, there are only a few reports (Payne *et al.*, 1947; Hermann, 1951; Dalgaard, 1954) describing the occurrence of thyroid cancer after its administration. This does not, however, exonerate thiouracil and similar drugs from having carcinogenic properties in man, because the latent period may be much longer than that covered by this study or since its introduction into medical therapy.

There are few reports in the literature dealing with malignant change in the thyroid gland after the therapeutic use of irradiation to the cervical region in adult life. In the present study only 4 (4.9%) of the 81 patients in whom it was possible to obtain information gave a history of previous *x*-ray therapy in adult life with a latent period of sufficient carcinogenic effect.

Similar observations have been made in a few cases by Kindler (1943), Quimby and Werner (1949), Wilson *et al.* (1958), and Goolden (1958). The paucity of such cases suggests that the adult thyroid may not be susceptible to radiation cancer. The papers by Quimby and Werner (1949) and Duffy (1957), reporting follow-up studies on patients who had received *x*-ray therapy for hyperthyroidism, lend credence to this hypothesis.

Summary and Conclusions

The incidence of thyroid cancer as a cause of death in necropsy and surgical material and its association with the various types of surgically treated goitre have been calculated.

Potential aetiological agents have been discussed and the following conclusions formulated: (1) Thyroid carcinoma is a rare finding at necropsy. (2) The incidence of carcinoma in specimens available for histological examination in this series is 4.1%. (3) Malignant change is more often associated with non-toxic nodular goitre than with toxic nodular goitre. (4) The diagnosis of thyrotoxicosis does not exclude the possibility of malignancy. (5) The frequency with which thyroid cancer is being diagnosed in surgical material is increasing. This is due to an increase in the total number of operations and to an increase in the number of operations for nodular goitre. (6) The use of antithyroid drugs in Northern Ireland does not appear to have influenced the increase of thyroid cancer. (7) The data at present available appear to give no indication that the adult thyroid gland is susceptible to radiation cancer.

I thank Professor J. H. Biggart for his advice and continued interest during the preparation of this work. I am indebted to Dr. J. E. Morison for his permission to include the material from the laboratories, Belfast City Hospital; and to all the consultants and general practitioners, whose names are too numerous for individual recognition, for their co-operation in answering the questionaries.

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CHLORPHENOXAMINE HYDROCHLORIDE IN PARKINSONISM

A CONTROLLED TRIAL

BY

P. R. ULDALL, M.B., B.S.
Late Senior House Officer

JOHN N. WALTON, M.D., M.R.C.P.
Assistant Physician

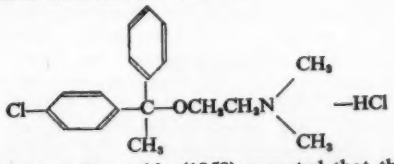
Department of Neurology, Royal Victoria Infirmary, Newcastle upon Tyne

AND

D. J. NEWELL, M.A., F.S.S.
Statistician, Department of Industrial Health, Medical School, King's College, Newcastle upon Tyne

The multiplicity of drugs available for the treatment of the Parkinsonian syndrome bears testimony to the fact that no single remedy has been found to be universally successful. Recent reports from the United States (Doshay and Constable, 1959; Magee and Currier, 1960) have suggested that chlorphenoxamine hydrochloride ("clorevan") is a useful addition to the remedies available, but up to the present time no results have been reported of controlled trials of treatment using this remedy and utilizing the double-blind technique. In this paper the results of such a trial conducted in a small series of patients are reported.

Chlorphenoxamine is closely related chemically to diphenhydramine hydrochloride ("benadryl") and has a chemical structure as follows:



Doshay and Constable (1959) reported that the drug appeared to be beneficial in 53% of a total of 169

patients who received it and who had failed to respond adequately to other forms of treatment. Magee and Currier (1960) concluded that the drug was of value in all of the clinical varieties of Parkinsonism, and they too found that approximately half of the patients to whom the drug was given were improved. In these two series of cases, however, no attempt was made to carry out a controlled trial, and the possibility of subjective error in the assessment of the results of treatment was therefore considerable. In each of these previous reports it was noted that chlorphenoxamine was much more successful in the control of akinesia and of rigidity than in the alleviation of tremor, which was not influenced to any significant degree. Magee and Currier pointed out that the drug did not seem to be as effective as benzhexol hydrochloride (" artane ") and procyclidine hydrochloride (" kemadrin "). In their view the primary value of the drug was as an adjuvant to other antispasmodic agents. They pointed out, as did Doshay and Constable (1959), that the drug was remarkably free from side-effects, the most severe being dizziness, which was encountered in a very small proportion of patients. It was also noted that the drug could safely be given along with large doses of other remedies without producing any cumulative ill effect.

Material and Methods

Twenty-seven patients with Parkinsonism accepted the invitation to take part in this trial, and after a full initial clinical assessment the purpose of the trial was fully explained to them. The only criteria for the selection of cases for inclusion in the trial were: (*a*) the diagnosis of Parkinsonism of the idiopathic or post-encephalitic types was incontrovertible; (*b*) the patients were already receiving a stable therapeutic regimen; and (*c*) it was important that the patients to be included in the trial should live near enough to the Royal Victoria Infirmary to be able to attend regularly for clinical assessment of the results of treatment. Of the initial 27 patients, 23 were accepted for inclusion in the trial; 4 were discarded because they did not fulfil the above criteria. Of the 23 patients who began the trial, 2 subsequently failed to attend for reassessment and the trial was continued with a total of 21 patients. Of these, 15 were suffering from paralysis agitans and 6 from post-encephalitic Parkinsonism. Eleven of the patients could be classified as being severely disabled by the disease, and the remaining 10 were moderately disabled.

Treatment.—The patients were instructed to continue taking the drugs they had previously been receiving, in exactly the same dosage as before, throughout the entire period of the trial. The drugs in question included benzhexol, benztropine methanesulphonate (" cogentin "), orphenadrine hydrochloride (" disipal "), and procyclidine in various combinations. It was arranged that throughout the period of the trial the patients should receive either chlorphenoxamine hydrochloride in a standard dose of 50 mg. three times daily, or dummy tablets which were identical in appearance and which were also to be given three times daily. Each patient was treated with chlorphenoxamine for three months and with dummy tablets for three months. The order of administration, chlorphenoxamine or dummy first, was decided from a list, based on random numbers, which was held in the hospital pharmacy. The randomization was restricted to produce nearly equal numbers starting on each treatment. Neither the doctor responsible for assessing the clinical response to treatment throughout the course of the trial nor the patient knew whether the chlorphenoxamine or the dummy was being administered at any one time. An interval of one week separated the two three-monthly periods, so that the effect of one treatment could wear off before the second treatment was begun.

Clinical Assessment

Each patient was assessed clinically, using criteria to be described below, before starting treatment, and one month and two months later during treatment. After a further month's treatment and an interval of one week without receiving either of the remedies, they were seen again, examined, and given the second treatment. Two examinations were made one and two months later while receiving the second treatment. At each visit the patients brought back any surplus of the tablets with which they had been supplied at the last visit. By this means a rough check was kept on whether they were taking the tablets regularly as prescribed. The patients' general practitioners were kept fully informed of the nature and purpose of the trial, and agreed to leave the previous treatment unchanged throughout its course.

The clinical assessment of the patients' condition was made by recording the following information at each visit. On each occasion the assessment was carried out by one of us (P. R. U.).

Subjective Impression.—Under this heading was recorded the patient's own impression of his clinical state during the preceding month. It was stated first whether he felt that he had been better or worse or much about the same during this period, and an attempt was made to discover whether he had been better able to dress or to feed himself, whether he had been walking longer or shorter distances than before, whether fine movements of his hands and his handwriting were improved, and whether there had been any alteration in akinesia or in speech and salivation. The patient's own account was supplemented by that of relatives who attended with him or her at each interview.

Rigidity.—This was assessed objectively for each of the four limbs at each visit on the following numerical scale: grade 1, normal tone; grade 2, slight rigidity; grade 3, moderate rigidity; grade 4, severe rigidity; grade 5, gross rigidity. The patient was given a numerical score for each limb according to this graduated scale, on each attendance.

Tremor.—This was similarly assessed objectively on a numerical scale as given below: grade 1, no tremor; grade 2, occasional and slight tremor; grade 3, continuous and slight tremor; grade 4, continuous and severe tremor, but controllable and abolished by activity; grade 5, continuous, severe, and uncontrollable tremor. The presence or absence of tremor and its severity according to this scale was again assessed numerically in each of the four limbs at each attendance.

Hand Test.—In this test a recording was made of the number of seconds it took the patient to make a fist and to open the hand completely again 10 times. At each visit the number of seconds taken for first the right hand and then the left was timed with a stopwatch. It was found that a normal person could carry out this series of actions within three to five seconds, but that a patient with severe Parkinson's disease could take up to 30 seconds.

Hence at each visit three measurements were taken—namely, measurements for rigidity in the arms and legs, tremor in the arms and legs, and the hand test—and the patients' subjective impressions were also recorded.

Results

Of the 21 patients who were admitted to the trial, four failed to attend one or more of the examinations

during treatment. The results which follow are based on the 17 who completed the entire course. Of the remaining four patients, one withdrew before receiving treatment with the dummy, two were marginally better on the chlorphenoxamine, and one was marginally better on the dummy remedy for all three criteria, on the occasions when they were recorded. Subsequent analysis has shown that inclusion of the partial records from these three cases would make no difference to the conclusions of the trial, and hence the findings in these patients have been excluded from further consideration.

Pre-treatment Results

The condition of the patients on admission to the trial is shown in the first two columns of Table I. The average rigidity score was 2.25 for the right arm and 2.21 for all limbs together. Tremor was more marked in the arms than in the legs, giving initial average scores of 2.76 for the right arm and 2.02 for all limbs. The average time to make a fist 10 times was 8.53 seconds for each hand.

TABLE I.—*Rigidity, Tremor, and "Hand-test" Scores; Pre-treatment Values*

Criterion	At Commencement of	
	First 3 Months	Second 3 Months
Rigidity—right arm	2·25	2·40
,, —4 limbs	2·21	2·28
Tremor—right arm	2·76	2·41
,, —4 limbs	2·02	1·84
Hand test	8·53	7·41*

* $P<0.01$.

At the end of the first three months' treatment, as already mentioned, an interval of one week without treatment was arranged before the next examination. It was expected that any effects of treatment would not persist beyond this time. The last column in Table I shows that the rigidity and tremor figures had not changed significantly from the initial value, but the patients were taking on an average one second shorter on the hand test. Further analysis shows that this improvement could not be attributed to persistence of the effect of treatment, since the improvement was present after both chlorphenoxamine and the dummy, and there was no significant difference between those who started on chlorphenoxamine and those who started on the dummy. We believe it must have been due to the patients becoming more used to the test (practice effect). The importance of having equal numbers beginning with active treatment and the dummy is obvious if practice in performing one of the tests resulted in improvement. In this trial eight patients began with chlorphenoxamine and nine began with the dummy. These numbers are close enough for the possible bias to be disregarded.

Criteria of Success of Treatment.—For each patient and each measurement two figures are available from the examinations one month and two months after the beginning of a particular treatment. The average of these two figures was taken to represent his functional ability while taking the treatment concerned. The difference between the two averages for chlorphenoxamine and for the dummy is the number used to indicate the superiority of chlorphenoxamine in that patient. For both rigidity and tremor the results were calculated for all four limbs together, and separately for the right arm only. The hand-test figures are the average of results on the two hands.

Analysis of Results

The results of the treatment are shown in Table II. Rigidity was on average slightly reduced and tremor slightly increased with chlorphenoxamine, but in neither case was the difference statistically significant. Comparison of Table II with Table I shows that, for these two criteria, neither treatment achieved an improvement over the initial state before treatment started. For the hand test, however, a significant difference was observed, patients on chlorphenoxamine clenching a fist 10 times in 6.88 seconds, compared with 7.66 seconds on dummy, an improvement of 10% in the time taken. This difference is not produced by the practice effect mentioned above. In fact, with only one more patient beginning on dummy than on chlorphenoxamine there is very little bias due to practice effect. Compared with the initial hand-test scores, the times were faster during each of the two treatments. The initial value of 8.53 seconds was reduced by 1.65 seconds on chlorphenoxamine ($P<0.01$) and by 0.87 second on dummy ($P<0.05$). On analysing the subjective impressions of the 17 patients during the course of the treatment it was found that seven had improved more with chlorphenoxamine, six had improved more with the dummy remedy, and four did not differentiate between the two treatments (in two of these cases there was a slight improvement on each treatment, and in the other two no change was apparent on either). Further analysis revealed that the subjective effect of chlorphenoxamine was no better in the severe cases than in those who were moderately disabled.

TABLE II.—*Effect of Treatment Upon the "Scores"*

Criterion (1)	Chlorphenoxamine (2)	Dummy (3)	Difference (4)=(2)−(3)
Rigidity—right arm ..	2·50	2·59	−0·09 ±0·17
,, —4 limbs ..	2·35	2·38	−0·03 ±0·11
Tremor—right arm ..	2·58	2·41	+0·17 ±0·12
,, —4 limbs ..	1·99	1·89	+0·10 ±0·06
Hand test	6·88	7·66	−0·78* ±0·29

* $P<0.02$.
Figures in columns 2 and 3 are averages of results one month and two months after starting the relevant treatment.
Standard errors in column 4 are based on within-patient comparisons.

Side-effects.—This trial has confirmed the almost complete absence of significant side-effects in patients treated with chlorphenoxamine hydrochloride. Throughout the entire trial period no significant side-effects were observed in any of the cases. It was, however, apparent that the addition of chlorphenoxamine hydrochloride in a dosage of 50 mg. three times daily to previous treatment, which was in several cases very substantial, did not appear to produce undue toxic reactions of any kind. Several patients who received this drug were already receiving as many as eight 50-mg. tablets of orphenadrine and two 2-mg. tablets of benztropine daily, and others were receiving as much as 20 mg. of benzhexol each day.

Discussion

The results of this trial are somewhat equivocal. Objective assessment revealed no significant reduction in muscular rigidity in patients who were receiving chlorphenoxamine, and tremor was actually increased in some, though this increase, too, was not significant.

However, it is clear that this drug, in the dosage given, has no significant influence upon tremor. It is also apparent, from an analysis of the subjective impressions of patients who were receiving the remedy, that almost as many patients were improved by the dummy as were improved by chlorphenoxamine. Hence if we base our assessment of the value of chlorphenoxamine in Parkinsonism upon the subjective impressions of the patients and upon our attempts to assess muscular rigidity objectively, our results do not indicate that, in the dosage we employed, this drug is of any real value if added to the previous treatment which the patient was receiving.

However, the objective evidence of the "hand test" did indicate that the patients' ability to open and close one hand rapidly was significantly improved by the administration of this drug. In our experience, too, this remedy is remarkably free from side-effects. On the basis of the hand test alone, therefore, it seems that there is some justification for suggesting that chlorphenoxamine is worthy of trial in cases of Parkinsonism if given along with other more powerful remedies. However, it is clearly not a powerful or highly effective remedy, and the results of our trial would justify equally the conclusion that, in the absence of any subjective improvement in the patients receiving treatment or of any measurable effect upon rigidity, the drug is of no therapeutic value.

Summary

A controlled trial of chlorphenoxamine hydrochloride in the treatment of Parkinsonism, using the double-blind technique, is described. Twenty-one patients began the trial and 17 completed the full course of treatment. Subjectively seven of these 17 patients improved more with chlorphenoxamine than with the dummy remedy, six improved more with the dummy, and four were unable to differentiate between the two treatments. Objective clinical assessment failed to reveal any significant effect of chlorphenoxamine upon rigidity and tremor, but this drug did produce a significant improvement in the ability to open and close the hands rapidly. No significant side-effects were observed in this series of cases.

We thank Dr. H. G. Miller for permission to include in this trial several patients who were under his care, and Mrs. Doris Weightman for assistance with the computations. We are also grateful to Dr. Arnold Worlock and to Evans Medical Supplies Ltd., who supplied the chlorphenoxamine and the dummy tablets.

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A new British Standard (B.S. 3330:1961) for polythene splints and appliances for external orthopaedic use has been prepared at the request of the Ministry of Health to ensure that correct materials are used in the making of the appliances, and to deal with those features of design which are independent of the clinical needs of each individual patient. The standard deals with appliances made of low-density polythene sheet, with or without a lining of cellular urethane. Basic information required for the fabrication of the appliances and notes on cleaning appliances are given in appendices. Copies may be obtained from the British Standards Institution, Sales Branch, 2 Park Street, London W.1 (price 5s. each. Postage extra to non-subscribers).

METHYL PHENIDATE IN PARKINSONISM

BY

A. M. HALLIDAY, M.B., Ch.B., B.Sc.

AND

P. W. NATHAN, M.D., M.R.C.P.

From the Neurological Research Unit of the Medical Research Council, National Hospital, London

It has been shown by Cole and Glees (1956) that the state resembling Parkinsonism which can be induced in the monkey by reserpine can be relieved by the sympathomimetic drug methyl phenidate hydrochloride ("ritalin"). Schneider and Holden have found that surgically induced tremor in the monkey can also be reduced by this drug (Carter and Maley, 1957). This suggests that the action of methyl phenidate is not specific to the reserpine-induced state and that it might be equally effective in similar types of disorder due to other causes. Glow (1959) reported that rats given reserpine go into a catatonic state, characterized by rigidity of the limbs and rhythmic alternating tremor of the head and neck; intraperitoneal methyl phenidate abolished the tremor and allowed the animals to run about and respond to their environment in a normal manner. In both monkeys and rats the effect of the injection of methyl phenidate was almost immediate and lasted some hours; the animals then reverted to the previous "reserpinized state."

In man, one of the main toxic effects of reserpine is to induce a clinical condition resembling Parkinsonism, and when given to patients with Parkinsonism the drug is reported to cause a marked though transient exacerbation of this disorder.

In view of these observations, and as methyl phenidate is satisfactorily absorbed when taken orally and is relatively non-toxic, we decided to try this drug in patients with Parkinsonism.

Accordingly, a pilot investigation was first carried out in which the drug was given intravenously to four male patients. This was followed by a more extended double-blind trial, in which the drug and control tablets were given orally to out-patients. Finally, those patients who in the blind trial were better on methyl phenidate were given various doses of the drug orally, either with or without their pre-existing medication, so as to find out the optimal dosage.

Results of Pilot Investigation: Intravenous Methyl Phenidate

For this part of the investigation, four male patients were chosen who manifested different forms of the disorder. Two were severely incapacitated, having been confined to wheel-chairs for some years; their movements were greatly impaired and were accompanied by very marked tremor and rigidity. The other two patients were much less severely affected and were still carrying on their respective occupations; the main disability in one was a dysarthria and in the other a coarse tremor of the right upper limb with minimal rigidity.

Each patient received a total of 30–40 mg. of the drug intravenously on each of one or two days, and this was usually given in two divided doses over a period of less than three hours. It caused a striking reduction in the rigidity, so that where rigidity impaired movements the

range and freedom of movement were greatly increased. One patient was able to get up from lying and to stretch his arms above his head, neither of which he had been able to do before. Subjectively the limbs felt less tense, and the patients performed spontaneous movements, the absence of which is usually such a typical feature of Parkinsonism. In the patient, however, in whom dysarthria was the main trouble and rigidity was relatively unimportant, there was a transient increase in tone in both upper and lower limbs on the side affected by Parkinsonism when a total dosage of 30 or 40 mg. was given. This passed off within 10 minutes and the limbs were then looser than normal as in the other patients. This transient hypertonia was not seen after a single dose of 20 mg. Speech appeared to be improved following methyl phenidate in all three patients in whom it was affected, becoming louder and clearer.

The drug had no beneficial effect on tremor, and in one patient the tremor became worse. The drug produced a lightening of mood in all four patients, with marked euphoria in two. In one, however, an initial period of cheerfulness was followed by a feeling of drowsiness and complaint that he felt dopy"; at this time the patient was quieter and more subdued than usual. Beyond this complaint and the presence of the transient hypertonia in one patient, there were no unpleasant side-effects other than slight lightheadedness or dizziness. Obvious effects of the drug lasted about two and a half hours after intravenous injection, but less obvious effects were still present a few hours later. One patient had insomnia on the night after the injection, and he noticed that his limbs were still definitely less rigid than normal the next day.

In view of the success of the drug in lessening rigidity and improving movement, and the likelihood that it would produce no undesirable side-effects when given in oral dosages limited to 20 mg., we decided to carry out a more extended trial to determine whether it would have a place as an adjuvant to other forms of medication in the long-term treatment of Parkinsonism. As it seemed clear that it had none of the beneficial effect on tremor of benzhexol hydrochloride, we did not feel justified in depriving patients of this drug for a number of weeks while the trial was in progress. Hence it was decided to test the value of methyl phenidate added to the existing medication.

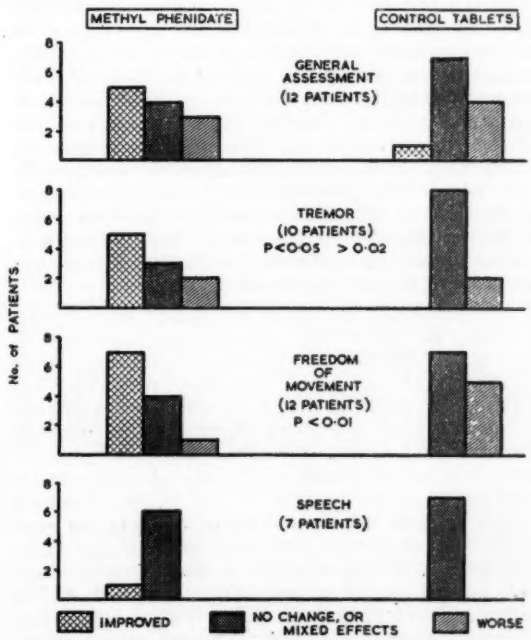
Extended Trial of Oral Methyl Phenidate

Twelve unselected out-patients with Parkinsonism were given the drug by mouth in addition to their usual medication. They attended the hospital once every four weeks, when they gave a report, were examined, and received a supply of tablets for the following month. The whole trial lasted 16 weeks for each patient, though one of the 12 gave up taking the tablets during the third month, complaining that they made her feel too ill. The tablets for any one month consisted either of 20 mg. of methyl phenidate or of excipient without any drug; neither the patient nor the doctor who assessed the patient knew which tablets were being given. In fact, each patient spent two months on methyl phenidate and two months on control tablets, the order in which these four were given differing from patient to patient. The patients were told to take two tablets on getting up and two after their midday meal; they were thus taking 40 mg. of methyl phenidate a day when on this drug. To avoid insomnia, the tablets were not given later in the day, and it was thought best to give them after lunch rather than before, because of the tendency of the drug to diminish appetite.

The patients were told that they were being asked to try out a new drug for Parkinsonism. They were asked at the end of each month how they had felt and whether they had noticed any change from the previous month. Sometimes they did note marked differences and asked for an explanation; they were told that for each of the four months they were receiving a slightly different form of the new drug, so as to see which was the best.

The assessment of the drug was based primarily on the patient's report. An attempt was made to supplement this with a more objective assessment, by clinical examination, and by using a battery of tests to try to detect and evaluate changes in the speed and dexterity of movement. Strength of hand-grip was tested with a dynamometer, and the acts of clenching and unclenching the fist, flexing and extending the elbow, knee, and ankle, 12 times each, were timed. The patients were also timed while they made a pile of six pennies, placing one on top of the other, one at a time, with each hand, and, again, while they removed 16 wooden pegs from holes in one side of a large board, turned the pegs upside down, and placed them in 16 holes on the other side of the board. Specimens of their writing (name and address) were taken on each occasion, and they also had to draw spirals and to attempt to guide a pencil down a zigzag groove 2 cm. wide without hitting the sides.

The results of this fairly elaborate objective assessment were unsatisfactory and disappointing. It was clear that times obtained in the tests of speed bore little or no relation to the speed of movement; many of the patients became stuck and unable to move at various points in the tests, and the length of these interruptions was much more variable, and often longer, than the total time taken by the test when it was performed



Results of extended trial with oral methyl phenidate.

uninterruptedly. Even apart from this, the movement and tremor in Parkinsonism are notoriously variable and easily influenced by emotional factors. It was clear that these tests gave little quantitative indication of changes occurring from month to month. They will therefore not be reported further.

Results of Trial

The results of the trial are summarized in the Chart. The patients' reports were rated for their overall opinion of the action of the tablets into three categories: definitely improved, definitely worse, and a third category, including both reports of no effect and mixed effects, good and bad. Similar ratings were made for the effect of the tablets on tremor, freedom of movement, and speech, including in each of the three groups only those patients in whom these were initially affected.

It is noteworthy that in this group of disabled patients, eagerly searching for drugs to help them, there was an unexpectedly slight degree of improvement reported with the control tablets. Only one of the 12 reported feeling generally better on them, while five of the same group felt a definite improvement while on methyl phenidate. None of the patients reported any definite improvement while on the control tablets in their individual ratings for freedom of movement, tremor, or speech, although at least half noticed improvement in movement and tremor on methyl phenidate. In only seven of the patients was speech affected, and only one of these reported any change while on methyl phenidate. This patient was the most severely dysarthric of the seven, and his speech was greatly improved while on the drug, as was obvious not only to himself but to the examining doctor. It became much louder, clearer, and altogether more intelligible.

Apart from any direct effect on motor function, a number of other differences were reported during the trial. Some of these may have been due to the pre-existing medication, or the combined effect of this with the drug, but in many cases these effects were quite clearly associated with the period during which methyl phenidate was being given, and did not occur with the control tablets. Among such effects were changes in mood (10 patients), sweating (3), subjective weakness (3), blurring of vision (2), dryness of the tongue (2), feeling generally unwell (2), palpitations (1), and anorexia (1). Two patients reported having transient symptoms immediately after taking the tablets—one of throbbing in the temples and the other of a "fluffy feeling with a kind of pins-and-needles all over." Four patients had no side-effects apart from those on mood.

The effect of the drug on mood was striking, although not all patients reported the same kind of change, and two noticed no effect on mood at all. Seven patients were stimulated, and three were adversely affected. However, in two of the latter group there was no real evidence of a swing of mood. They were the two patients already mentioned who felt generally unwell on methyl phenidate, one of whom gave up the trial during the third month for that reason. The third patient reported that she felt quieter mentally and more contented and that the pills made her tired and sleepy for about 10 minutes after she had taken them. There was no such report by her during the periods on the control tablets, so that this effect must be regarded as a genuine effect of the drug. The seven patients whose mood was lightened by the drug felt less tired and had more energy than before; they wanted to be "on the go," and some were frankly restless or excited. In two of the patients the increased cheerfulness was very marked. Some of the patients found this upward swing of mood the best single effect of the drug, while others did not like it.

After they had completed the blind trial, all the patients, with the exception of the two who had felt ill on the drug, were put on methyl phenidate, in most cases combined with other medication, and the dose was individually adjusted. Six of the 10 patients felt better on the drug than without it (including one ranked as having shown "mixed effects" in the blind trial). Several of these patients were extremely enthusiastic about the drug, which one called the best she had tried; another patient said that on it he felt better than he had done for years. They all wished to go on taking the drug indefinitely. The effects observed were the same as those in the main trial. The individual dosages arrived at ranged from 30 to 100 mg. daily, usually in two divided doses taken on rising and after lunch. In the four patients who obtained no benefit from the drug in the blind trial there was also no benefit with increased dosage.

Discussion

The results of this trial can be summarized by saying that half the patients tested felt better on methyl phenidate, though some of its beneficial effect was not derived from specifically anti-Parkinsonian features of its action, but from the fact that it gave the patients more energy and lightened their mood. However, there appears to be no doubt that it also increased freedom of movement and reduced tremor and rigidity in a number of these patients, and, although it improved speech in only one of the seven affected patients, its effect here was obvious and occurred in the most severely dysarthric of the group. A quarter of the patients tested were no better on methyl phenidate and a quarter felt definitely worse. The drug was obviously less effective when given orally than when given intravenously in the dosages used.

Although many of the patients reported that the tremor was improved on the drug, neither in the intravenous nor in the oral trial did any patient show the striking abolition of tremor reported in the animal experiments which led us to undertake this trial. This was disappointing; but it may not be surprising when the dosages used in the monkey and rat are compared with those which we employed. Cole and Glees (1956) injected 20 mg. subcutaneously (equivalent to 6.6 mg./kg. body weight in an average 3-kg. monkey), and Glow (1959) 10 mg./kg. in the rat. If we assume a mean weight of 70 kg. for our subjects, they were given something between one-twentieth and one-fortieth of the equivalent animal dose. Unfortunately, though the drug is relatively non-toxic, we had ample evidence of the occurrence of unpleasant side-effects even with these dosages, so that it does not seem practicable to increase the dose of the drug further, to try to reproduce in man the total abolition of tremor and rigidity with complete restoration of normal co-ordination and activity which the animals exhibited. It is still an open question whether this effect would be produced with any dosage in Parkinsonism, but it would seem well worth while for pharmacologists to try to produce a variant of the drug without its undesirable side-effects, which would be even more effective against tremor and rigidity.

Summary

Methyl phenidate (" ritalin ") was given to patients with Parkinsonism. Four patients received it intravenously and 12 received it orally in a double-blind trial; those patients who obtained benefit from the drug given orally then received it in various doses, alone or in combination with other medication for Parkinsonism, in order to establish the optimal dosage.

The drug gave some patients an increased freedom of movement and reduced the rigidity; it had little effect on the tremor. The most marked effect was the improvement in mood.

Our thanks are due to Dr. E. A. Carmichael for his interest and encouragement, and to the physicians of the National Hospital who kindly allowed us to include in this trial the patients under their care. We would like also to thank Dr. C. D. Falconer, of Ciba Laboratories Ltd., who supplied us with the drug and control tablets.

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Preliminary Communications

Pyloric Stenosis: A Physiological Exploration

Pyloric stenosis is a common condition in infancy, occurring in three to four of every thousand newborn infants (Davison, 1946). The clinical syndrome is well defined, but little information is as yet available concerning the physiological changes. In the present study intragastric pressures have been measured as a reflection of the motility of the fundus of the stomach in nine infants with pyloric stenosis. The fundus as opposed to the antrum was chosen as it shows little if any activity in health, so that a more definitive change might be expected in this area. The method has shown a clear difference between normal infants and those with pyloric stenosis.

In most cases the diagnosis presents little difficulty; it rests on the finding of a typical pyloric tumour in a vomiting baby. However, Craig (1955), using accepted criteria for his physical signs, found a pyloric tumour in no fewer than 25 out of 115 symptom-free babies whom he examined when less than 2 weeks of age. Contrary to accepted opinion, he concludes that a palpable tumour in a baby during the first two weeks of life is not necessarily diagnostic of pyloric stenosis. The clinical condition of pyloric stenosis clearly must depend on a disturbance of function and not on the presence of a tumour.

Methods.—The technique of measuring intra-oesophageal pressures in infants has already been described (Colley and Creamer, 1958). A similar method was used for recording intragastric pressures. The pressures were measured through fine water-filled " polythene " tubes connected to Hansen capacitance manometers beside the child. Two tubes were used, fastened at the tip and with lateral recording holes spaced 3 cm. apart. The tubes were passed through the mouth and positioned so that the proximal recording hole was just below the hiatus of the diaphragm, a point which can easily be recognized by the reversal of inspiratory pressure swings. The recordings in most instances were made immediately after a feed or during and after a feed.

CASES STUDIED

Nine infants with pyloric stenosis were studied and their clinical features are summarized in Table I. The age at onset ranged from 2 to 6 weeks. All presented

TABLE I.—*Clinical Data on Cases with Pyloric Stenosis*

Case	Sex	Position in Family	Birth Weight lb.	Birth Weight g.	Age at Onset (Weeks)	Vomiting	Constipation	Weight Loss	Palpable Tumour	Peristalsis	Treatment
1	M	4	8·5	3,770	6	+++	0	++	+	+	Operation
2	M	2	6·8	3,085	5	+++	+	+	+	+	,,
3	M	3	9·3	4,220	2	+	++	++	+	+	,,
4	M	2	9·4	4,265	6	++	+	+	+	0	,,
5	F	1	6·13	2,780	4	+	0	+	+	+	Medical
6	M	1	5·15	2,335	3	+	+	0	+	+	,,
7	M	3	6·12	2,775	4	++	+	+	+	+	Operation
8	F	3	7·13	3,234	4	+	0	0	+	+	,,
9	M	1	6·7	3,040	4	++	0	+	+	+	,,

with vomiting, though in only four could it be described as projectile. Constipation was noted in five cases, but in two there were loose " hunger stools." Loss of weight occurred in all but two babies, and in one case resulted in the infant being 12 oz. (340 g.) below his birth weight at 3 weeks of age.

A pyloric tumour was felt in all cases and peristalsis was observed in eight. Rammstedt's operation was performed in seven cases and resulted in the immediate cessation of symptoms in six. In the other infant (Case 8) the pyloric muscle had not been adequately split and the infant continued to vomit. Two cases were treated medically with atropine methonitrate (" eumydrin ").

The control group contained six cases. Three were infants who were studied because of vomiting due to causes other than pyloric stenosis—infection, air-swallowing, etc. The others included the sibling of a child who had had pyloric stenosis but was free from symptoms, a baby with Fallot's tetralogy, and an infant that was slow to gain weight but appeared otherwise normal.

RESULTS

Classification of Activity.—There is no available classification for activity of the fundus of the stomach as there is for the antrum. Two types of pressure change are seen. Most commonly this is a simple wave of pressure, usually occurring rhythmically from two to three times a minute. Where this is 5 cm. of water-pressure or less we have arbitrarily called it a type I wave; where more than 5 cm. of water-pressure, a type II wave. Occasionally these waves are superimposed on a general rise in pressure lasting up to two minutes and ranging in amplitude from 2 to 12 cm. of water-pressure. These base-line variations have been called type III waves. In every record the pressure tracings from the two recording sites in the fundus were identical.

Findings in Control Subjects.—There was no difference in the records from normal children and children vomiting from causes other than pyloric stenosis (Table II). The recordings were conspicuous for the lack of

TABLE II.—*Summary of Recordings from Control Cases*

Case	Vomiting	Time Activity Present	No. of Waves	Type of Waves I	Type of Waves II	Type of Waves III	Amplitude (cm. Water) Max.	Amplitude (cm. Water) Mean
A	+	27%	23	23	0	1	2	1·7
B	+	12%	5	5	0	0	2	1·4
C	+	0%	0	0	0	0	0	0
D	0	22%	4	4	0	0	3	2·3
E	0	0%	0	0	0	0	0	0
F	0	12%	5	5	0	0	2	1·4

activity (Fig. 1). In two children there was no activity whatsoever, and in the remainder activity was present from 12% to 27% of the time. This activity consisted of small undulations of pressure ranging from 1 to 2 cm. of water; only one wave was recorded of 3 cm. of water-pressure and none above this. The waves usually

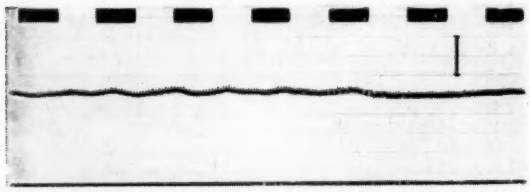

FIG. 1.—Recording from one tube in the fundus of a control infant. In all figures time is marked in 30 seconds and calibration = 20 cm. water pressure.

occurred in short rhythmical bursts ranging from 1.5 to 3 a minute. Only one type III wave was recorded of 2 cm. of water pressure.

Findings in Untreated Pyloric Stenosis.—The outstanding feature in the records was that marked activity was present for most of the time (Fig. 2, Table III). In two cases the activity was continuous throughout the records and in the rest it varied from 45% to 74% of the time. Where recordings were made during feeding, activity began either during or immediately after the feed (Fig. 3) and continued during the whole time of observation (maximum, ½ hour). Most of this activity was of rhythmically occurring type I or II waves. These waves corresponded in timing to the presence of visible peristalsis but were sometimes present when peristalsis

TABLE III.—*Summary of Recordings from Cases with Pyloric Stenosis*

Case	Time Activity Present	No. of Waves	Type of Waves			Amplitude (cm. Water)	
			I	II	III	Max.	Mean
1	74%	14	0	14	2	19	13·4
2	100%	17	1	16	2	35	18·4
3	54%	9	5	4	0	16	6·3
4	100%	54	21	33	2	27	8·3
5	50%	5	2	3	0	8	5·8
6	60%	4	3	1	1	6	4·2
7	45%	14	10	4	0	20	4·5
8	54%	16	2	14	4	27	14·6
9	71%	27	21	6	0	12	4·0

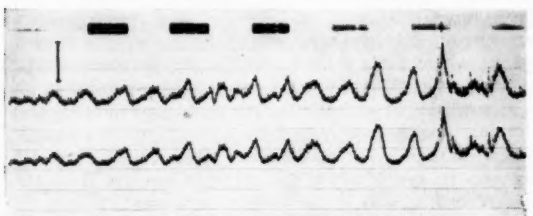

FIG. 2.—Recording from two tubes in the fundus of Case 4. Note the continuous activity.

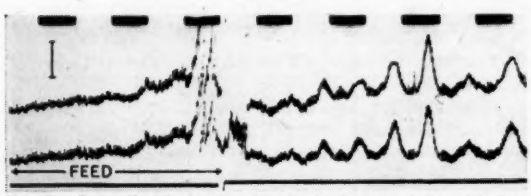

FIG. 3.—Recording from two tubes in the fundus of Case 8 before operation. Note the activity beginning after the feed and increasing in amplitude.

could not be seen. Peristalsis was never seen in the absence of pressure waves. The pattern commonly seen was for activity to begin during or after the feed as small type I waves, and gradually to increase in amplitude—type II waves—and in one instance this ended in a projectile vomit (Fig. 4). In every case type II waves were present, ranging in maximum amplitude from 6 to 35 cm. of water-pressure, and in most cases there were waves over 15 cm. of water-pressure. The rhythmicity of these waves varied from 1.8 to 3.6 a minute. Type III waves were present in five of the nine records. In a few instances the tubes were repositioned so that one tube was recording from the lower oesophagus and the other from the fundus. During many vigorous waves the cardia remained competent and there was no pressure change in the oesophagus. However, during a few waves the appearance of oesophageal reflux was seen.

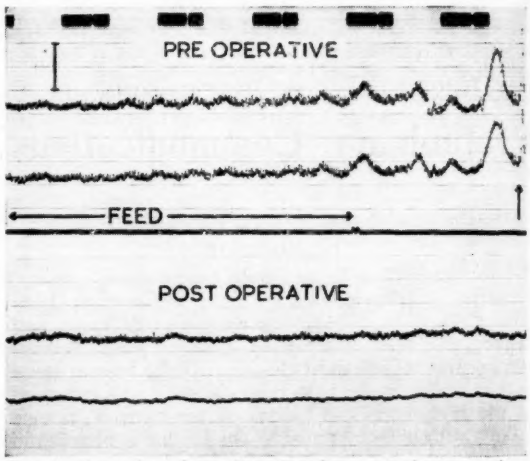

FIG. 4.—Recordings from Case 7, before and after operation. In the pre-operative record the activity increases after the feed and terminates in a projectile vomit, indicated by the arrow. The post-operative record is taken after a feed and shows little activity.

Findings After Rammstedt's Operation.—Post-operative records were obtained from five infants; four of these had a good clinical response to surgery, while one was a failure in that vomiting continued. None of the recordings were completely normal (Table IV). In one

TABLE IV.—*Summary of Recordings from Post-operative Cases*

Case	Result	Time Activity Present	No. of Waves	Type of Waves			Amplitude (cm. Water)	
				I	II	III	Max.	Mean
1	Good	28%	6	5	1	0	7	3·3
2	,,	2%	1	1	0	0	5	—
7	,,	27%	6	6	0	0	4	3·0
9	,,	51%	8	0	8	2	17	12·0
8	Failed	80%	18	12	6	1	35	8·4

infant there was a great reduction in the amount of activity with only one wave, but this was of higher amplitude than any recorded in the controls. Two others showed an appreciable modification of the original pattern, but in one of these waves up to 7 cm. of water-pressure were present (Fig. 4). One infant (Case 9) showed a good clinical result, but the pressure trace was very little different from the pre-operative one. In the failure (Case 8), the record was again little changed, showing more activity but less average amplitude (Fig. 5).

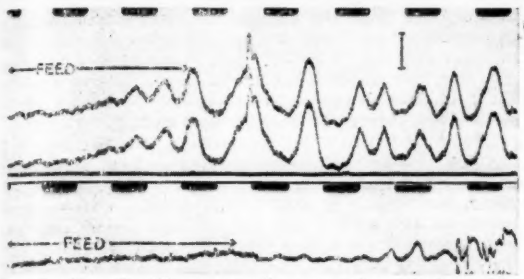

FIG. 5.—Case 8. Upper recording was taken 14 days after operation, when vomiting was persisting. Lower recording was taken after atropine methonitrate had been used for two days.

Effect of Drugs.—In Case 8, failed Rammstedt's operation, several recordings were made in the post-operative period to follow the progress and estimate the effect of drugs. The first two recordings, taken at 7 and 14 days after operation, showed unabated activity. After this atropine methonitrate, first as a liquid, "eumydrin" m.5, and later as lamellae, "pylostropin" 1/750 gr. (0.087 mg.), was given before feeds. Recordings after these showed a large reduction in the amount of activity and amplitude of the waves (Fig. 5).

DISCUSSION

Tracings from the antrum of the stomach by balloons or open-tipped tubes show waves that can be demonstrated by radiology to contact the lumen so that a localized activity in the muscle coats is being recorded. In the fundus of the stomach this does not apply; the tubes lie in a sac, and pressure changes may be due to local or generalized activity which almost certainly does not contract down so as to obliterate the lumen. This means that pressure tracings must be interpreted with caution. It might be argued that the pressure waves in infants with pyloric stenosis come from augmented antral contractions and not the fundus. That the fundus is capable of this activity in adults is shown by the presence of similar activity in the gastric pouch of patients after partial gastrectomy (Creamer and Hindle, 1960, unpublished observations).

The results show a clear-cut difference between normal and vomiting infants and cases with pyloric stenosis both in the amount of activity and in the amplitude of the waves recorded. Waves over 5 cm. of water-pressure were seen only in pyloric stenosis. The method has been used in diagnosing the cause of neonatal vomiting with success. Similar tracings have been obtained from adults with acquired pyloric stenosis.

After operation the pattern is usually modified, but at the time of recording (5 to 10 days) it has not fully returned to normal and may be almost unchanged. This argues either that the effect of obstruction takes some time to wear off or that pyloric stenosis is a disturbance of motility not confined to the pylorus but involving the whole of the stomach. In Case 9, in which a good result was obtained, the record was almost unchanged at nine days after operation, suggesting that a generalized abnormality of motility may be more likely.

SUMMARY

Pressures in the fundus of the stomach have been measured in nine infants with pyloric stenosis and six infants who had no evidence of the disease. A constant abnormal pattern of increased activity was present in all cases of pyloric stenosis. This is modified by operation, but does not return to normal within the first 10 days.

B. CREAMER, M.D., M.R.C.P.,
Physician and Senior Lecturer in Medicine.
D. G. COTTOM, *M.C.*, B.M., M.R.C.P., D.C.H.,
Paediatrician.
W. HINDLE, M.B., B.Sc., M.R.C.P.,
Medical Registrar.
St. Thomas's Hospital,
London.

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Medical Memoranda

Bilateral Rupture of Achilles Tendons

Rupture of the Achilles tendon is seen more often in a younger age-group. In a series of 92 patients, Arner and Lindholm (1959) found that the average age was 38.5 years; the youngest was 23 and the oldest 72. Sections from specimens removed at operation showed that degenerative changes in the Achilles tendon were a prerequisite to rupture, so that the ease with which rupture is brought about would appear to depend on whether or not the degenerative changes were far advanced.

The mechanism of the injury is usually sudden dorsiflexion of the plantar-flexed foot or violent active plantar flexion as is common in sport. The patient gives a history of having felt a sudden sharp pain in the heel and falls to the ground. There is rarely a history of pain at the heel for any length of time prior to the rupture. The following case differs in several respects from this classical picture and is for that reason worth recording.

CASE REPORT

A man aged 68 who had suffered from chronic bronchitis and asthma for several years was referred in August, 1960, complaining of pain above both heels for four months. For his respiratory disease he had been treated with a variety of drugs, and for the past 16 months these had included methylprednisolone. The dosage of that drug had ranged from 2.5 mg. t.d.s. up to 10 mg. t.d.s., and in the four months before he was referred he had been taking 4 mg. t.d.s.

Just prior to his being seen he noticed that the pain above his left heel had disappeared, but he did not recall any trauma or painful incident associated with its disappearance.

On examination he was found to have a rupture of his left Achilles tendon with a palpable gap, the tear having taken place about 3 cm. above its insertion. On the other side no abnormality could be detected to account for the pain. In the course of the examination he was asked to stand on his toes—on the good side first. To my astonishment there was a resounding crack and he fell to the floor. Examination confirmed that he had ruptured his remaining Achilles tendon; a palpable gap was present.

He had only slight pain, which quickly passed off, and he was able to walk about the room quite comfortably within a few minutes—indeed, he insisted that he could make his own way home unaided.

He was seen subsequently on several occasions, and reported that after the second ruptured tendon he had had no further pain around the heels. The ruptured tendons were no disability, as he was unable to walk quickly because of his respiratory disease.

COMMENT

Spontaneous rupture of tendons may result from pyogenic infection, tuberculosis, gonorrhoea, syphilis, gout, or tumours (Boyd, 1938), and is seen not infrequently as a part of the clinical picture of rheumatoid arthritis. In the latter condition the tendons undergo fibrinoid degeneration, a characteristic of the collagen diseases. It is possible that in the present case the pain prior to the final tendon rupture was due to minute tears in the degenerating tendon, and that normal healing was inhibited by the steroid therapy. In an experimental study Wrenn, Goldner, and Markee (1954) showed that, though end-to-end healing of ruptured tendons in animals on cortisone therapy was not prevented, the tendons were 40% weaker than control tendons. The cortisone delayed the maturation of the fibrous tissue. The ease with which the tendons ruptured in the present case and the relative lack of pain at the time would indicate that they were grossly degenerated.

A similar picture is seen at the shoulder, where again a large tendon mass is involved. In the older age-group rupture of the supraspinatus tendon occurs with relatively little trauma and minimal pain. In a slightly younger age-group chronic tendinitis is seen which is painful and may be the sequel to a partial tear (Apley, 1959). This would perhaps correspond to the pain in the present case during the four months before the tendons ruptured.

I am grateful to Mr. E. A. Devenish for his helpful criticism.

G. B. SMAILL, M.B., Ch.B., F.R.C.S.,
Orthopaedic Registrar, West Middlesex Hospital, London.

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Simultaneous Bilateral Rupture of Achilles Tendons Due to Triamcinolone

Cramps, muscle-wasting, and myopathy are well-known complications of corticosteroid therapy. They occur most commonly with triamcinolone (Dubois, 1958; Kendall and Hart, 1959; Neustadt, 1959), but have also been described after cortisone (Perkoff *et al.*, 1959), prednisone (Harman, 1959), fludrocortisone (MacLean and Schurr, 1959), and dexamethasone (Duvenci *et al.*, 1959; Golding and Begg, 1960). The following case is of interest, as the patient developed simultaneous bilateral rupture of the Achilles tendons as a sequel to triamcinolone therapy, given for chronic discoid lupus erythematosus (chronic L.E.).

CASE REPORT

A 52-year-old scaffolder was first seen in the department of dermatology in October, 1957, with a 14-year history of chronic L.E. of both cheeks. He was treated initially with chloroquine, 400 mg. daily, but some activity of the lesions remained; and by August, 1958, he was complaining of blurred vision and "spots in front of the eyes." Hydroxychloroquine sulphate was substituted for chloroquine in daily doses of 800 mg., and this was subsequently increased to 1,200 mg. and then 1,600 mg. daily, as response was not complete.

A lichenoid eruption of the legs was noticed in December, 1958, while he was on hydroxychloroquine only. In view of this, and since the chronic L.E. was still active, the hydroxychloroquine was stopped and triamcinolone begun in doses of 4 mg. twice daily and increased to four times daily two months later. Both the discoid lesions and the lichenoid eruption had cleared completely by March, 1959; however, he then complained of night sweats.

Clinical and chest *x*-ray examinations were negative, and the dose of triamcinolone was reduced to 4 mg. three times daily. On April 28 he was seen in the orthopaedic department because of pain in both Achilles tendons which interfered with his climbing ladders. No abnormality was found either in the tendons or in the ankle-joints. At this time he could walk fairly well and was treated by strapping both ankles. On May 12 he complained of cramps in both calves, worse on the left, and because of this triamcinolone was gradually reduced during the next six days and mepacrine, 300 mg. daily, substituted. On May 21, three days after triamcinolone had been stopped, he noticed pain in his left ankle, and a short time afterwards his right ankle was also painful when standing on a ladder. He had not exerted himself unduly. Walking was now almost impossible, since he could not plantar-flex his feet properly. He was taken to hospital, where a diagnosis of rupture of the Achilles tendons was made. Surgical repair was carried out a fortnight later by Mr. R. G. Taylor under A.C.T.H. cover, and recovery was uninterrupted. He has regained normal functions of both tendons.

Because of a relapse of his skin condition, oral prednisolone was started in June, 1960, and by December he was receiving 5 mg. twice daily; the chronic L.E. was inactive again and there were no untoward effects.

COMMENT

Since simultaneous rupture of both Achilles tendons is very rare, it seems probable that it was caused by triamcinolone, and that it was not due to the lupus erythematosus. The patient complained of cramps in his calves and tendon pain four weeks before treatment was stopped. It is probable that partial rupture was present at this stage, since it has been shown (Anzel *et al.*, 1959) that a tendon will continue to function apparently normally when 75% of its fibres are ruptured. Arthritis, tenosynovitis, syphilis, and tumour are no longer regarded as being significant aetological factors in this condition; however, there must be some abnormality of the tendon before rupture can occur. Characteristic degenerative and necrobiotic changes have been found in tendon tissue examined within 24 hours of rupture, which presupposes that they must have been present before (Arner *et al.*, 1959). It has been suggested that these changes are ischaemic and are secondary to hypertrophy of the media and narrowing of the lumina of medium-calibre blood-vessels. Triamcinolone almost certainly aggravated, if not initiated, these changes in our case.

We thank Dr. H. R. Vickers for permission to publish this case.

M. A. COWAN, M.B., M.R.C.P.,
SUZANNE ALEXANDER, M.B., B.S.,
Department of Dermatology, United Oxford Hospitals.

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Reviews

SURGERY OF ACUTE ABDOMEN

Surgery of the Acute Abdomen. By John A. Shepherd, V.R.D., M.D., Ch.M.(St. And.), F.R.C.S.Ed., F.R.C.S.Eng., Q.H.S. Foreword by Sir Zachary Cope, M.D., M.S., F.R.C.S. (Pp. 1,228+x; illustrated. £5.) Edinburgh and London: E. and S. Livingstone Ltd. 1960.

There is real need for a book of this kind on acute abdominal surgery, and Mr. Shepherd has compiled an extremely comprehensive and clear work which will commend itself to a wide circle of readers. The arrangement of the subject-matter follows orthodox lines. The format, printing, and illustrations are of a high order. Each chapter is generously interlarded with useful clinical descriptions of the author's personal cases, all of which add substance and clarity to the text. An appendix lists the author's personal emergency operations during a fourteen-year period, and it is plain that he has not only put in a tremendous amount of hard work on his patients but has also devoted much time and thought to research on his case material. What little such a book must sometimes lack from not reviewing the material of a whole hospital, or statistics from other collective sources, is more than compensated for by the analysis of cases whose problems must live vividly in the mind of the writer.

A historical review at the beginning of each section is most useful, and often helps to put present-day practice in proper perspective. An excellent bibliography is found at the end of each chapter, and every reference is included in the preceding text. Such an excellent book can withstand one or two minor criticisms. In the chapter on post-operative complications references to the dosage of heparin are rather vague and inaccurate. The oral anticoagulants are stated to require control by estimation of "clotting time," and the process of clotting is sometimes confused with that of thrombosis. Jejunogastric intussusception is referred to as a "rapidly progressive condition" necessitating urgent operation, but most surgeons must have seen this more often as a less dramatic condition. Atelectasis is frequently printed as "atalectasis."

Notwithstanding these possibly churlish criticisms, this is a fine book and a very great credit to the author. It can be strongly commended to all surgical registrars and surgeons who deal with acute abdominal emergencies.

R. S. MURLEY.

BLOOD DISEASES IN THE YOUNG

Blood Diseases of Infancy and Childhood. By Carl H. Smith, M.A., M.D. (Pp. 572; illustrated. £6 7s. 6d.) St. Louis: The C. V. Mosby Company. London: Henry Kimpton. 1960.

This book, Professor Carl Smith tells us, is designed to present the salient features of blood diseases against the background of normal development in infancy and childhood, a background that must be appreciated if correct diagnoses are to be reached. It is meant to be a companion to larger textbooks, "since few diseases in this or other specialities can be arbitrarily restricted to a specific age period." It presents an extremely comprehensive account of the blood diseases and includes accounts of relevant diseases of the spleen, the reticuloendothelial system, and the "malignant lymphomas."

After short general chapters, the individual diseases are dealt with at length. Naturally most attention is paid to the diseases that are specially important to paediatricians, and there are detailed accounts of erythroblastosis foetalis, and the indications for exchange transfusion, the anaemias of prematurity, the haemoglobinopathies, the aplastic anaemias, and the leukaemias of childhood. There are some chapters of particular interest on transfusions in paediatric practice, and on the difficult subject of the differential diagnosis of jaundice in the neonatal period; a comprehensive list of the bone and joint manifestations of the blood diseases of infancy and childhood is provided. Valuable tables showing the changes with age of many blood values are scattered throughout the book, including one showing the serum iron and iron-binding capacities at various ages. Iron-deficiency anaemia itself is very thoroughly discussed since it is common and important, and we are glad to note that Professor Smith states categorically that cobalt, copper, molybdenum, folic acid, and vitamin B_{12} are not needed for the treatment of iron-deficiency anaemia in childhood.

The book is very up to date and many recently described syndromes are included—for example, pyridoxine deficiency anaemia, the chronic benign granulocytopenia of childhood, Aldrich's syndrome of eczema, thrombocytopenia and anaemia, and the anaemias associated with enzyme deficiencies in the red cells. Chronic nonspecific infectious lymphocytosis, the so-called "low-fever syndrome," will be news to many and help to explain the course of illness in many patients suspected of having lymphatic leukaemia. The section on blood coagulation is clear and practical. There are fifty illustrations, mostly photographs showing blood films, histological sections, radiographs, and some clinical pictures illustrating such disorders as skin rashes; they are helpful and not over elaborate. Coloured illustrations of blood and marrow cells have been left to the atlases. At the end of each chapter a good selection of references is provided.

This is a very good book; every page is informed with the clinical judgment and critical assessment that can only come from extensive experience. It is one of the few haematological books that will be read and used for constant reference, a book in fact that everyone interested ought to own. It is all the more to be regretted that the price should have been fixed so high; its 572 pages, with no colour illustrations, cost more than the 1,185 pages of Wintrobe's comprehensive textbook.

M. C. G. ISRAËLS.

EPIDEMIOLOGICAL METHODS

Epidemiologic Methods. By Brian MacMahon, M.D., Ph.D., Thomas F. Pugh, M.D., M.P.H., and Johannes Ipsen, C.M., Dr.Med., M.P.H. (Pp. 302; illustrated. 55s.) London: J. and A. Churchill Ltd. 1960.

In this book the authors study the underlying principles of epidemiology. The term epidemiology is used in its modern concept and includes the non-infectious diseases as well as the infectious epidemic diseases, and much of the book is illustrated by examples from statistics of chronic disease. No statistical knowledge is demanded of the reader and no statistical techniques are discussed. The sources of mortality and morbidity data, the measurements used for comparative purposes, and the effect of age, sex, ethnic group, marital state, occupation, social class, etc., on the mortality and sickness experience are reviewed. No mention is made of the life table as an epidemiological tool. The advantages and disadvantages of the various indices

are discussed at some length. These discussions are generally well balanced and unbiased, and, in particular, the reasons for and against cohort analysis as compared with current age rates are given in detail. The causes of variation in the disease pattern from place to place and within a country are discussed, and the effect of biological, physical, and social environments are outlined. The changes in clinical diagnosis, concepts, terminology, and in classification over the years and their effect on time trends and the difficulties of interpretation are reviewed. In the two chapters on analytic epidemiology in which the retrospective and forward study are compared the authors are, perhaps, a little too optimistic about retrospective studies, since often this type of study does not yield satisfactory data.

The authors, who are members of the department of epidemiology of Harvard University, have largely succeeded in their object of presenting the principles of epidemiology in a manner that can be easily understood by the general reader who has no prior knowledge of the subject. Although this book is not a textbook in the usually accepted sense, the reader who wants to learn something of the broad basic principles of epidemiology will find it an instructive and readable book.

W. J. MARTIN.

TROPICAL MEDICINE REVIEW

International Review of Tropical Medicine. Edited by David Richard Lincicome. Volume I. (Pp. 300+xii; illustrated. $10.) New York and London: Academic Press. 1961.

The *International Review of Tropical Medicine* has been founded to provide critical reviews of knowledge of diseases that affect man or animals in tropical climates. There is a widely representative international editorial board ranging from Jerusalem to Djakarta, from Teheran to Mexico. There are seven contributions to this first volume: three from the United States of America, three from Great Britain, and one from Holland.

Pride of place is given to an opening article by R. G. Cochrane, the leading British leprologist, who gives a general account of the present position of classification, pathology, and treatment of leprosy, and goes on to put forward a powerful plea for the establishment of a world centre "which would serve as a power house for the stimulation of research, teaching, and training in leprosy throughout the globe: a registry of histopathology and a reference laboratory where the variegated patterns of leprosy could be appreciated." This comes most aptly at a time when Cochrane's unique collection of specimens and slides is in danger of leaving Britain, and the suggestion is referred to by the editor as "a noble idea."

Charles Wilcocks, of London, contributes a useful article on "Sources of Information in Tropical Medicine," a discipline which, as he points out, embraces most human diseases but which requires an extensive knowledge of zoology and of other related disciplines. He points out that reviews like the *International Review* form an important and essential bridge between original publications and final textbooks.

Sir Philip Manson-Bahr adds to his collection of Mansoniana by a characteristic contribution on Manson as a parasitologist, which, though it is hardly in keeping with the nature of the *Review*, will interest a younger generation unfamiliar with the achievements as a naturalist of the father of tropical medicine.

E. C. Faust, of New Orleans, ranges over the many controversial aspects of *Entamoeba histolytica* infection. He reviews the experimental methods used to determine the pathogenicity of both large and small races of amoeba, but in the end "goes out by that same door wherein he went." He provides a very comprehensive bibliography of an important subject on which much work remains to be done.

H. A. P. C. Oomen, of Amsterdam, contributes a well-documented authoritative review of xerophthalmia with a wealth of fine illustrations. He points out that, despite much advance in our knowledge of vitamin deficiencies, a great deal of accurate investigation is called for. Each case of xerosis of the cornea should be treated as an emergency, but even when the vitamin A deficiency has been overcome treatment is anything but finished, and the order of sequence of medical action should regard first the eye, second the patient, and third the kitchen. Normal fish liver oil should be the remedy of choice. Carotene should not receive too much single emphasis in propaganda—the importance of fat and protein should be stressed simultaneously.

M. Goldman, of Georgia, U.S.A., writes on fluorescent antibody research, pointing out that this ingenious and extremely useful method has up to the present time made little impact in the tropical field. Goldman deals briefly with techniques, and suggests modes of application of this method in the study of viruses, rickettsiae, bacteria, fungi, protozoa, and even helminths—particularly in connexion with micro-filariae.

H. Hoogstraal, of the U.S. Naval Department, writes on "Ticks and Tick-Borne Diseases: Some International Problems and Co-operation in Their Study." His contribution is of great general interest, and should make some readers realize that so far as tick-borne disease is concerned there is no such thing as an island, as investigation of scrub typhus demonstrated in the Indian Ocean in 1943. "Millions of migrating birds, rapidly flying between continents, may be virus-infected and tick-infested." Ticks are unique in their ability to harbour and transmit a great variety and number of pathogenic organisms. In reviewing the present attempts by international organizations to broaden our knowledge of tick-borne diseases Hoogstraal states that the considerable advancement made towards the goal of improving human health and wealth stimulated by several international agencies is a measure of progress of civilization and science.

It is difficult for an internationally edited book of this nature to be absolutely up to date, but this opening number leads one to believe that we have in this *Review* a useful new instrument for the dissemination of knowledge, though the price, 10 dollars, is rather high.

GEORGE R. MCROBERT.

PLASTIC SURGERY CONGRESS

Transactions of the International Society of Plastic Surgeons. Second Congress, London, 1959. Edited by A. B. Wallace, M.Sc., F.R.C.S.Ed. (Pp. 589+xxiv; illustrated. 90s.) Edinburgh and London: E. and S. Livingstone. 1960.

This volume, ably edited by A. B. Wallace, forms a record of the 1959 International Congress of Plastic Surgeons held in London under the presidency of Rainsford Mowlem, and contains the manuscripts of 91 papers delivered by contributors from all parts of the world. As is to be expected, the papers (all in English) vary very much in style, material, and quality. They have been arranged in 16 sections, which virtually divide this book into chapters and add greatly to its orderliness. Each paper is followed by summaries in French,

German, and Spanish. It is obviously impracticable to deal here in any detail with this extensive material; the wide range of topics which in their diversity impinge on almost every branch of surgery emphasizes the breadth of field encompassed by the plastic surgeon. There is something in this volume to interest surgeons in all specialties.

The section on cleft-lip and cleft-palate surgery is the largest and most embracing. There are nine papers on various aspects of the problem of homografting, and eleven on hand surgery, including Littler's ingenious method of restoring sensation to the contact area of an anaesthetic digit with an island pedicle. Surprisingly enough in the section on burns only four papers were read. In the general field of reconstructive surgery the trend is evidently towards transplantation of living tissue rather than the insertion of fabricated materials, references to which are very much in a minority in this collection of papers.

Because of the time factor, 111 papers were "read by title" only, and these are listed at the end of the book; as such, this list is of little value to the reader, and it is a pity that space could not have been found for a short summary of the essential content of each paper.

The arrangement of the material and the general standard of illustration is excellent. Although not cheap, the price compares very favourably with that of many other similar congress transactions, especially as the volume is so well produced.

J. WATSON.

BRADFORD'S DR. EURICH

Dr. Eurich of Bradford. By Margaret Bligh. (Pp. 295. 25s.) London: James Clarke and Co. Ltd. 1960.

The author of this biography, Dr. Eurich's daughter, is quite right in stating that the people of Bradford owe a great deal to him. His labours, his discoveries, his triumphs, and his many years of painstaking work will not, and, indeed, must not, be forgotten.

Few men can have been so unassuming or so antipathetic to open praise; few have been such a Jack of all trades and yet so complete a master of so many skills. Mrs. Bligh divides her father's biography into several separate yet interdependent sections. The story of the fight against anthrax, for instance, is an epic, rivalling in interest Bruce's battle with malaria and the mosquito, but Dr. Eurich never got the full credit that he deserved for his victory. His theories on penal reform and the treatment of delinquents, both old and young, his recognition that mental breakdown may often be connected with physical illness, were years before their time; it is only now, long after his death, that we can see how right he was on so many points.

In these days of super-specialism in medicine it is good to read of a doctor who treated his patient as a whole human being, as an individual, and not just as a case, of a doctor who took infinite pains to study his patient from every angle, medical, psychological, and social, and who was not prepared to skimp any detail that might lead him to a positive method of helping his patient as well as to an accurate diagnosis. Dr. Eurich's art was not a fortuitous gift, it developed through sheer hard work and scrupulous attention to detail—here the Germanic strain in his ancestry came in—combined with an astounding memory.

The book is full of well-told anecdotes, illustrating Dr. Eurich's family life and work and sketching very adequately the times in which he lived. Mrs. Bligh has written a fascinating story of a truly remarkable man, as his daughter she well knew the great man, his strength and his weaknesses. Every one, in or out of Bradford, will benefit from reading *Dr. Eurich of Bradford.* To the student of British medicine it provides a stimulus for further research into our methods and an example of complete dedication to the cause of suffering humanity.

J. C. A. DOWSE.

CLINICAL MEDICINE AND BASIC SCIENCES

Disease and the Advancement of Basic Science. Edited by Henry K. Beecher. (Pp. 416+xi; illustrated. £5.) London: Oxford University Press. 1960.

There is to-day a tendency, quite rightly, to emphasize the debt which clinical medicine owes to the basic sciences, and indeed many recent advances are related directly or indirectly to skills, techniques, and attitudes of mind stemming from the more exact disciplines of chemistry and physics. On the other hand, less acknowledgment is given to the contribution that clinical observation has made to the advancement of scientific knowledge, and there can be little doubt, for example, that the sum of human physiological knowledge has been advanced in many fields more by the scientifically trained physician than by the professional physiologist.

In this volume are collected twenty-one lectures by distinguished American scientists, and each one makes exciting and interesting reading. In his contribution "Molecular Structure and Disease" Linus Pauling discusses the different haemoglobin molecules, how this knowledge has grown from the clinical study of sickle-cell anaemia, and the protection against malaria afforded to sickle-cell heterozygotes with one haemoglobin-S gene. Alexander Bearn gives a scholarly account of the "Contribution of Clinical Medicine to Biochemical Genetics"—a field which is still only at the dawn of its great importance and future. Who better than Dickinson Richards could discuss "Cardiovascular Physiology," or William B. Castle "Advances in Physiology Derived from the Study of Anaemia in Man"? Among less expected topics is a chapter on "Deformities as Cues to Understanding Development of Form" by Paul Weiss. In an age when the physician—even in a full-time academic appointment—has difficulty in keeping abreast of progress in fields removed from his own special interests this sort of book provides a rewarding scientific and philosophic stimulus which cannot fail to widen his horizons.

R. I. S. BAYLISS.

METABOLISM OF TUMOURS

The Glycolysis and Respiration of Tumors. By Alan C. Aisenberg. (Pp. 221+xiii. $8.) New York and London: Academic Press. 1961.

Science and medicine are continuously in search of all-embracing hypotheses and explanations for their manifold problems. In this way it is hoped to unify the multiple aspects and tidy up untidy ends. Sometimes such an approach is very successful, as in the cases of infectious diseases or the cellular basis of histopathology, but at other times concept-making is less successful, especially when a single name has been given to morbid states which in fact form a whole group of diseases. This has happened with "cancer," where the desire for a possible common denominator or, even more so, for

a common cure has been so strong that it has sometimes ignored the sober reality of facts.

More than thirty years ago Warburg offered a theory which he thought would explain the basic nature of the malignant state of cells. It referred to the possibility that the cancer cell in comparison with its normal counterpart suffers from an impaired respiration and consequently develops another means of producing energy—namely, the fermentative one—which is also known as the glycolytic pathway. Over the years a great number of reviews, summaries, and criticisms have been written, articles published, even whole books have been printed, to assess the validity and significance of the Warburg concept.

Recently Dr. Aisenberg has produced a monograph in which he restates the whole problem of energy metabolism of tumours, and, supported by numerous references to experimental work in the field, discusses its implications. In a brief but concise fashion he touches on all aspects: the anaerobic and aerobic glycolysis of normal and tumour tissue, the oxidative metabolism of tumours, the so-called Pasteur and Crabtree effects representing regulation of respiration and glycolysis, and the dependence of tumours on oxidative and glycolytic energy. He comes to the conclusion, as others did before him, that, while tumours have a high glycolysis rate and a somewhat marginal respiratory apparatus as compared with a great number of normal tissues, there is no compelling evidence—so he says—to place the energy metabolism of tumours in the central position of the neoplastic process. This is regretted because of the pressing need for a rational approach to the chemotherapy of cancer. This is expressed by Aisenberg, who finishes his excellent monograph with the following words: "At the present time, it is not possible to say . . . that the cancer cell can or cannot be controlled by a selective chemotherapeutic attack on its energy metabolism." Translated into action, this means more work for the biochemist, histologist, and experimental pathologist, who are also expected to pay more attention to the problem with regard to human cancers.

F. BERGEL.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Coronary Vasodilators. By R. Charlier. (Pp. 208+xi; illustrated. 55s.) Oxford, London, New York, Paris: Pergamon Press. 1961.

Handbook of Research Methods in Child Development. Edited by Paul Henry Mussen. (Pp. 1,061; illustrated. £6 2s.) London: John Wiley and Sons. 1961.

The Red Cell. By T. A. J. Prankerd, M.D. (Pp. 184; illustrated. 32s. 6d.) Oxford: Blackwell Scientific Publications. 1961.

Antibiotica et Chemotherapia, Vol. 9. Edited by O. Gsell and R. L. Mayer. (Pp. 188. Sw. Fr. 40.) Basle, New York: S. Karger. 1961.

Age is Opportunity. (Pp. 203. 8s. 6d.) London: The National Council of Social Service. 1961.

Les Techniques Sociométriques. By Georges Bastin. (Pp. 184. No price.) Paris: Presses Universitaires de France. 1961.

Lipide Metabolism. Edited by Konrad Bloch. (Pp. 411. 84s.) New York, London: John Wiley and Sons, Inc. 1961.

Fearon's Introduction to Biochemistry. Edited by W. J. E. Jessop, M.D., M.Sc., F.R.C.P.I., D.Ph., F.R.I.C. (Pp. 473. 30s.) London: William Heinemann Medical Books Ltd. 1961.

Die Erkrankungen der Gallenwege und des Pankreas. By Walter Hess. (Pp. 672; illustrated. DM. 142.) Stuttgart: Georg Thieme Verlag. 1961.

Quantitative Methods in Pharmacology. Edited by H. de Jonge. (Pp. 391; illustrated. 84 guilders.) Amsterdam: North Holland Publishing Company. 1961.

IXth International Congress of Radiology (Proceedings). Vols. I and II. Edited by B. Rajewsky. (Pp. 1,625; illustrated. DM. 240.) Stuttgart: Georg Thieme Verlag. Munich and Berlin: Urban and Schwarzenberg. 1961.

La Méningite Purulente Traitée. By Pierre Mozziconacci and François Girard. (Pp. 247. NF. 39.) Paris: Masson et Cie. 1961.

Memory, Learning, and Language. Edited by William Feindel. (Pp. 69; illustrated. 16s.) University of Toronto Press. 1961.

Learning to Love. By Alan H. B. Ingleby. (Pp. 142. 10s. 6d.) London: Robert Hale Ltd. 1961.

Gefässwand und Blutplasma. Edited by R. Emmrich and E. Perlick. (Pp. 250; illustrated. DM. 44.80.) Jena: Veb Gustav Fischer Verlag 1961.

The Public Health Inspector's Handbook. By Henry H. Clay, F.R.S.H., F.I.P.H.E. (Pp. 673; illustrated. £2 15s.) London: H. K. Lewis and Co. Ltd. 1961.

Milk: the Mammary Gland and its Secretion. Vols. I and II. Edited by S. K. Kon and A. T. Cowie. (Pp. 515 and 423. £5 and 86s.) New York and London: Academic Press. 1961.

Listeriosis. By H. P. R. Seeliger. (Pp. 308; illustrated. Sw. Fr. 55.) Basel and New York: S. Karger. 1961.

Der menschliche Lymphknoten. By Bernfried Leiber. (Pp. 474; illustrated. DM. 248.) Munich and Berlin: Urban and Schwarzenberg. 1961.

Robert Koch und Sein Werk. By Johannes Kathe. (Proceedings of the German Academy of Sciences in Berlin.) (Pp. 60; illustrated. No price.) Berlin: Akademie Verlag. 1961.

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CONCUSSION IN CHILDREN

Head injuries in children are increasing in frequency. Many are due to falls, and an increasing number are a result of road accidents,[1] which constitute a serious social problem. In 1959 more than half the admissions of children to hospital as a result of injury were admitted because of head injury.

The child has a relatively elastic skull and intracranial vessels, and the brain appears to tolerate injury and to have greater powers of recovery than in the adult. Minor head injuries are more frequent in children than in adults, and in boys than in girls.[2] Though greater reorganization of neurological function appears to be possible in the young, a minor head injury in a child may cause a much more dramatic syndrome than in an adult. Initially there may be unconsciousness, the child may be pale, and vomiting and seizures may appear. He is often restless, and rapid changes in the clinical picture are rather common. Thus careful interrogation of witnesses and careful clinical observation and recording are required.

Certain differences in the consequences of concussion between children and adults are illustrated in a paper by H. Dillon and R. L. Leopold.[3] They report on fifty children, seen over a two-year period, who had sustained head injuries, mainly from motor accidents. The duration of unconsciousness was not known in 35 cases. Forty-seven had psychological changes such as aggressiveness, antisocial behaviour, a tendency to withdraw from society, deterioration of school work, anxiety symptoms, and hyperkinesis. Sleep disturbances and enuresis were also common. The typical adult post-concussional syndrome, which includes headache, dizziness, vertigo, irritability, tinnitus, poor memory, and fatigue, was rarely seen. Epilepsy occurred in eight patients, five with grand-mal and three with petit-mal seizures; four of these patients had normal electroencephalograms. Of eighteen patients with no clinical evidence of epilepsy, eight had abnormal tracings and were considered likely to develop it.

Several of the patients had cerebral contusion, fracture of skull, and subarachnoid haemorrhage. Accident-proneness was not important in the group. This series was a specially selected group in that each patient was referred by a lawyer for a medical report. By contrast, in Britain medico-legal intervention for children who have had concussion is rare.

In a recent paper W. B. Jennett and Walpole Lewin[4] discuss epilepsy after closed head injuries. They found that epilepsy, early and late, after trivial head injuries was confined to children. In comparison with the child's brain the adult's brain appeared to require more severe damage (amnesia for some hours) to produce epilepsy. The incidence of epilepsy in those under 5 years of age was almost twice that in other groups. The possible reasons were—that the brain is more susceptible at an early age; children at this age are often closely observed by their parents and admitted to hospital; and a latent tendency to epilepsy may be brought to light by the brain trauma. All but one of their series of 822 patients (all ages) who had developed "early epilepsy" did so within a week of injury, which emphasizes the need for careful observation of these patients.

Some argue[5] that a "post-concussional syndrome" does not exist. Certainly many patients with obvious organic brain damage do not necessarily show any special post-traumatic symptoms. But if psychological symptoms develop after a head injury in a child they usually differ from those seen in adults. Thus, G. F. Rowbotham and colleagues[6] described the effects of head injury in 82 patients under the age of 12 years. Twenty-seven had a change in temperament, with nervousness, lack of concentration, faulty memory, bad temper, and enuresis. Some psychological difficulties may go undetected because of the difficulty in communication that children may have. S. J. Dencker carried out an interesting study[7] of 128 consecutive patients with closed head injuries in persons of twin birth, examining them 3 to 25 years after their accidents; he used the co-twins of the same sex as control subjects. An insignificant lowering of results on psychometric testing of monozygotic twins was found. The severity of concussion and its prognosis may be gauged from the duration of post-traumatic amnesia, but this is difficult if not impossible to estimate in younger children. As to the psychological outcome of children who have had cerebral concussion, the pre-traumatic personality and factors in the child's environment appear to be more important than the nature and severity of the head injury.

[1] *Road Accidents*, 1959. H.M. Stationery Office.
[2] Harris, P., *Arch. Dis. Childh.*, 1956, **32**, 488.
[3] Dillon, H., and Leopold, R. L., *J. Amer. med. Ass.*, 1961, **175**, 86.
[4] Jennett, W. B., and Lewin, W., *J. Neurol. Neurosurg. Psychiat.*, 1960, **23**, 295.
[5] Pond, D., *Cerebr. Palsy Bull.*, 1960, **2**, 246.
[6] Rowbotham, G. F., Maciver, I. N., Dickson, J., and Bousfield, M. E., *Brit. med. J.*, 1954, **1**, 726.
[7] Dencker, S. J., *Arch. gen. Psychiat.*, 1960, **2**, 569.

Possibly about 10–15% of all patients admitted to hospital because of a head injury require operative treatment in one form or another, but operative treatment is only rarely required for minor head injuries in children. The main complication, though fortunately not common, is the development of an intracranial haematoma, particularly an extradural one. After concussion this may cause symptoms leading to unconsciousness with or without a "lucid interval," or there may be no initial spell of unconsciousness. Certain danger symptoms and signs, such as persisting headache, vomiting, restlessness, irritability, a dazed state, drowsiness, changes in the vital signs, an ipsilateral, dilated, poorly reacting pupil and a contralateral hemiparesis, may develop over a period of minutes or hours; indeed, before the condition is diagnosed the patient may already be comatose and show signs of the decerebrate state. Epilepsy is not an early sign of a developing extradural haematoma. The most important feature in these patients is a deteriorating state of responsiveness. All patients with concussion or a period of amnesia after a head injury should be carefully observed in a hospital for 24–48 hours. Special investigations are of limited value, but a radiograph of the skull may show a fracture which might have injured a middle meningeal artery. The electroencephalogram is difficult to interpret in the young and it is often normal in cases of concussion, though Dillon and Leopold[3] stress its value as a diagnostic aid. However, they say that the psychological sequelae in these patients are probably of more clinical importance than the organic disturbances, because the electroencephalograms usually revert to normal, while the psychological symptoms will persist.

Psychological tests are also of limited value in the diagnosis of brain damage after minor head injuries in children. Dillon and Leopold believe that reassurance and mild tranquillizers are often sufficient for children who have been concussed, but state that intensive psychotherapy is sometimes indicated; and they advise anticonvulsant therapy when evident seizures have occurred, or when electroencephalographic changes are found, or indeed when there are hyperkinetic symptoms. Few clinicians in Britain would agree that anticonvulsants should be routinely used in these patients unless clinical epilepsy had occurred. When the patient is unconscious his airway must be maintained, and this can usually be achieved simply by placing him on his side.

Though cerebral concussion is common in children, it usually follows a benign course, so that few of them require or receive neurosurgical care. Poor results in the treatment of extradural haematoma in children are usually due to delay in instituting treatment—that is, timely evacuation of the haematoma and control of the haemorrhage. Unless serious psychological abnormalities or physical complications have arisen as a result of concussion, the patient should be got up, sent home, and allowed to return to school without unnecessary delay. It may be worth taking special care to keep the child quiet for a time, but this is not often possible.

CHOLERA

Cholera is still a common disease in the East. Its true home, where it is permanently endemic with annual epidemic outbreaks, is the east of India and East Pakistan. Thence it tends to spread, mainly inside India, and mainly to places of religious assembly, where the pilgrims normally take ritual baths in the very source of their water supply, but it also crosses ocean barriers to become epidemic in other Asiatic lands. Between 1947 and 1959 there have been large epidemics in Burma, Nepal, Cambodia, and Thailand, the last-named having suffered 11,555 cases in 1958 and 7,777 in 1959. Small outbreaks have occurred in Ceylon, Goa, Laos and Vietnam, but none have been recorded in other continents since the 1947 epidemic in Egypt. Yet cholera used to be an epidemic disease of Europe and North America: London epidemics were used by Snow to prove the waterborne transmission of disease, and the very terror of its name acted as the genesis of international disease control. Pilgrims still pass through Egypt, the Sudan, and Arabia in vast numbers, and an aeroplane can transfer an infectious person half-way round the world overnight. Dysentery and typhoid are common enough in Africa, and not so very uncommon in the United Kingdom. Why should the most savage of all alimentary infections be so easily confined?

One major reason is that the chronic carrier of *Vibrio cholerae* is virtually unknown. "Only acute carriers, that is, individuals late in the incubation stage, those actually ill, and possibly also those in early convalescence, are instrumental in spreading the infection."[1] Then, in order to flourish, cholera requires a combination of dense population and abysmal sanitation, almost always in relation to a river that acts simultaneously as water supply and sewer. Though flies and contaminated food play important parts in transmission, the provision (and use) of safe water supplies have always led to the

[1] Pollitzer, R., *Cholera*, World Health Organization Monograph No. 43, 1959. Geneva.

extinction of cholera. The essential features of the true endemic areas are that they are low-lying (less than 500 feet above sea level), hot, and humid, and have a very high water table. The construction of safe wells is a difficult problem, and even if it is surmounted there is surface water everywhere, from which people traditionally draw their drinking-water.

The statistics of the last 12 years show a great and consistent decline in the incidence of cholera throughout India, especially in the epidemic areas (Madras had 26,171 deaths in 1948, and 150 in 1959) but also in the endemic areas. In East Pakistan the annual deaths have dropped from 29,582 in 1948 to 12,735 in 1959, though even the latter figure gives little cause for rejoicing. The installation of safe water supplies is the best preventive of cholera, but vaccination has played a great part in stopping its spread. Since vaccination became compulsory for international travel in affected areas, cholera has been conspicuously absent from countries involved in the Mecca pilgrimage, and the improvement in areas such as Madras is largely attributed to the vaccination of travellers. Ideally, and compulsorily for "pilgrims," two doses of cholera vaccine should be given at 7 days' interval. Owing to the practical difficulty of maintaining contact with pedestrian travellers only one dose is usually given, but the evidence suggests that, though this does not provide complete individual protection, it does lower the susceptibility of the total population to infection sufficiently to prevent epidemics. Cholera, then, is a preventable disease, coming from a permanent focus in the eastern part of the Indian peninsula. Why is it not prevented by mass vaccination? The present answer to this question can be surmised from the figures for that even more readily preventable disease, smallpox. In the same areas as those of endemic cholera, West Bengal and East Pakistan, in 1958 there were respectively 27,372 and 48,043 cases of smallpox. To vaccinate on the scale required to prevent these diseases requires money, time, staff, and, above all, the co-operation of the population.

POSTGRADUATE DEVELOPMENTS IN LONDON

A newspaper headline[1]—"New Postgraduate Medical School for London"—may have given readers the impression that the Ministry of Health had in fact reached the conclusion that a new postgraduate medical school was to be set up in addition to the well-known Postgraduate Medical School at Hammersmith. So far as we understand the position this is not the case. According to *The Times* report on June 2, St. Luke's Hospital will be closed, and the plans which have been discussed by the South-west Metropolitan Regional Hospital Board and the Ministry of Health will affect the Royal Marsden Hospital, the Brompton Hospital, and the Chelsea Hospital for Women. And a leading article in *The Times* of June 5 questions the apparent choice for this change of what is described as "the Brompton Road complex of hospitals."

It would seem that this startling piece of news is a jump ahead of any final conclusion that may yet be reached by the Ministry of Health in discussions with hospital boards. If it is possible to read between the lines of a story that is not yet complete, we think it is unlikely that any new postgraduate medical school will be established in London. But for some time now there has been disquiet about the buildings and facilities of the various postgraduate institutes in London, one of which is, of course, associated with the Brompton Hospital for Diseases of the Chest, to give it its full title. If work in these postgraduate institutes is hampered by out-of-date buildings and facilities that do not match up with modern medicine, then any review of existing inadequacies would obviously have to take into account the location of these institutes in different parts of London. The logical step, therefore, would seem to be to group the existing institutes in one or more centres in London, and to take advantage of what opportunities may be offered for this by strengthening the position of London as one of the great world centres for post-graduate training and research. This would provide a knotty set of problems for the many institutes involved, not least among which will be the present high value of property. Speculation about possible sites for the regrouped institutes might at this juncture turn out to be misleading, but at least it is safe to say that no new postgraduate medical school is being contemplated.

[1] *The Times*, June 2, 1961.

ANTIMONY AND THE HEART

Describing the effect of sodium antimony tartrate on the myocardium, M. Honey[1] records his cardiological findings in 59 patients under treatment with sodium antimony tartrate in London during two years. Of particular importance was the death of two young West African women, ascribed to the toxic action of the drug on the myocardium. One of these patients (aged 23 years) collapsed and died unexpectedly at the end of an 18-day course of treatment, during which she had 29 gr. (1.9 g.) of sodium antimony tartrate. The other

[1] Honey, M., *Brit. Heart J.*, 1960, **22**, 601.
[2] Aragao, H., and Vianna, G., *Arch. bras. Med.*, 1913, **3**, 1171.

(aged 21 years) died equally suddenly after 23 gr. (1.5 g.) had been given over 12 days. Necropsy revealed a concentration of antimony in the myocardium ten times that in the blood.

The introduction of parenteral antimony treatment for South American visceral leishmaniasis[2] was a landmark in the development of the chemotherapy of parasitic infections. Potassium antimony tartrate was given intravenously. Within a remarkably short time it was shown, in India and elsewhere, that intravenous administration of this drug was specific in the treatment of the other forms of kala-azar, and in Egypt that it was specific in the treatment of the two forms of schistosomiasis so prevalent there. It was early appreciated that treatment with tartar emetic was attended by many inconveniences, and also that it might entail grave risk to the patient. The inconveniences were due to the violently irritant nature of the solution, which had to be introduced with scrupulous care into the veins, since a severe local necrosis followed its escape into the surrounding tissues. The risks were due to the general reactions which took place even while the solution was being introduced. On occasions sudden death occurred during the course of treatment.

The sodium salt of antimony tartrate is generally held to be rather less toxic than the potassium salt, and to-day is usually given in preference to it. More complex organic compounds of antimony, in both the trivalent and the pentavalent forms, have also become available. These, particularly the latter, are comparatively non-irritant and can safely be given parenterally by other than the intravenous route; the immediate systemic reactions due to them are much less frequent and severe than those from tartar emetic. For kala-azar some of the pentavalent antimonials have proved therapeutically superior to any of the trivalent antimonials, even tartar emetic. The adoption of these pentavalent antimonials, together with non-metallic synthetic preparations such as those of the diamidine series, has eliminated tartar emetic from use in the treatment of visceral leishmaniasis.

In schistosomiasis, on the other hand, the pentavalent antimonials unfortunately have proved valueless as therapeutic remedies. Some synthetic trivalent antimonials do exert a schistosomicidal action, and have been employed widely for the treatment of the disease; further, there are some non-metallic synthetic preparations which can be given as an alternative to these antimonials. Unhappily, the plain fact remains that no drug at present available equals, or even approaches, tartar emetic as an efficient schistosomicide. Some patients infected with *Schistosoma haematobium* (urinary schistosomiasis) may successfully be treated with one of the alternatives, but tartar emetic remains the most consistently curative drug for this infection. In the management of cases of *S. mansoni* (intestinal schistosomiasis) infections the inferiority of the alternatives, antimonial or non-metallic, is much more notable; and the same applies in even greater degree to *S. japonicum* infections (Far Eastern schistosomiasis). As no case of schistosomal infection in man can be ignored, in view of the cumulative effects of an active parasitization which persists for over 20 years, the tartar emetic treatment must still be used in spite of its difficulties and dangers.

During the last twenty years greater attention has been paid to the pharmacology of tartar emetic and other antimonials and particularly to their effect on the heart. Sudden death or cardiovascular collapse may occur at any time during treatment with tartar emetic, and this may be due to idiosyncrasy to the drug. But electrocardiographic studies show changes that progress during the treatment of every patient. These changes vary in their intensity with the individual, and it appears that they are more pronounced in Africans and in Asians than in Europeans. They are not limited to those under treatment with tartar emetic but are also seen, albeit to lesser degree, in patients being treated with the other trivalent antimonials. The damage appears to be to the myocardium. Honey notes that Chinese workers treating *S. japonicum* infections with potassium antimony tartrate have observed a high incidence of serious ventricular arrhythmias, but these have not been reported elsewhere. The electrocardiographic changes are not permanent, and the recordings return to normal progressively over about two months after cessation of the antimony treatment.

Honey recommends that an electrocardiographic recording should be made on all patients under treatment with tartar emetic when the first 15–20 gr. (1–1.3 g.) of the drug has been given. If the recording is distinctly abnormal the dangers of continuing the drug treatment must fully be appreciated. It is much to be hoped that the long-sought safe alternative for the treatment of schistosomiasis will be forthcoming in the not-too-distant future, but until it is we have to continue to use tartar emetic.

ENDOCRINE OPERATIONS FOR BREAST CANCER

It is remarkably difficult to make a true estimate of the relative values of adrenalectomy and hypophysectomy in the treatment of metastatic breast cancer, and there are signs that the initial enthusiasm for these operations is giving way to doubt about the indications for them.[1] One obvious reason for this state of affairs is that no group of observers publishing their own results can base their conclusions on populations of adequate size.

There may not be as many varieties of breast cancer as there are victims of the disease, but if cases were classified according to the intrinsic growth rate of the tumour, as determined by clinical rate of progress of the disease, the number of its biological varieties would be large, and small populations of cases of inadequate size would prove to be biologically heterogeneous. On this basis some attempt must be made to study breast cancer in populations large enough to compensate for the wide variation in the lethality of the growth, and thereby achieve reasonable biological homogeneity.

[1] *Brit. med. J.*, 1961, **1**, 646.
[2] A Preliminary Statement by the Joint Committee on Endocrine Ablative Procedures in Disseminated Mammary Carcinoma, *J. Amer. med. Ass.*, 1961, **175**, 137.

A preliminary report[2] of such an attempt has recently come from a committee of experts jointly appointed by the American College of Surgeons and the American College of Physicians. The records of 871 cases from eleven centres where endocrine ablation is under close investigation were made available to the committee. The only selection exercised was to discard cases having incomplete records. In each accepted case the committee formed its own conclusions on the success or failure of the operation, and after careful statistical analysis of the case histories they were satisfied that by pooling the results in this large population and examining them in retrospect they had achieved reasonable biological homogeneity.

Their main conclusions are shown in the following table:

	Adrenalectomy	Hypophysectomy
Total number of cases	404	467
Post-operative deaths	9·1%	9·0%
Objective regression of growth longer than six months	31·7%	31·3%
Mean post-operative survival (in months):		
With growth regression	22 months	20·6 months
No ,, ,,	6·5 ,,	7·0 ,,

This preliminary report provides no evidence of superiority in effectiveness of either operation over the other, and obviously indicates that adrenalectomy is likely to be of wider usefulness than hypophysectomy. The full report of the committee will in all probability dispel much of the confusion to which previously published evidence appears to have given rise.

SUICIDE NOTES

Suicide notes have recently received some attention from research workers. They reflect a variety of feelings and motivations. Some ask for forgiveness, others for love which has been withheld. Many are accusatory and vindictive and lay the blame for the suicide at somebody else's door. Invariably they aim at eliciting certain emotional responses from survivors who had been close to the victims. Sometimes society at large is blamed. W. Morgenthaler's[1] collection of suicide notes obtained at Berne is the only monograph on this subject, but the author did not analyse their contents. The question whether there is something peculiar about the people who leave these notes, or about their suicidal acts, had not been investigated until recently, when a group of American psychologists directed their attention to this problem. They found that in Los Angeles county 12 to 15% of those who committed suicide left notes behind. The note-writing group did not differ in socio-economic status from the others. E. S. Schneidman and N. L. Farberow[2] compared genuine with simulated suicide notes. The control group consisted of healthy persons, carefully matched for age and other features, who were instructed "to write a suicide note as they might write it were they planning to take their lives." Thirty-three paired notes were reproduced and it was left to the reader to pick out the real from the faked, though a key with the correct solutions was provided. The verbal contents of these same notes were subjected to a careful grammatical and psychological analysis by L. A. Gottschalk and G. C. Gleser.[3] They found that the genuine notes showed more references to persons, things, and spatial relationships than the faked ones. While cautious in their interpretations, these investigators believe that such notes reveal "an unusual preoccupation with objects of the live world and, by inference, a wish to maintain some tie with or produce some persistent effect on such objects." They suspect the suicidal person who writes a note to differ in this respect from the others. However, as these authors themselves wondered, it is questionable whether the instructions given to the healthy group could produce a state of mind comparable to that in which suicide is committed.

In Great Britain observations reported by A. Capstick[4] are in keeping with those of the American workers. Investigating a large sample of suicides in Wales, he found that 15.4% had left notes behind. Those under 60 were more inclined to note-writing than older people. Capstick observed that the notes sometimes showed a striking preoccupation with the things of this world, which contrasted oddly with the wish to die. He also remarked that these people had the urge to influence the attitudes of survivors towards them. Only one of his 136 note-writers showed an indifference to life. All the others were intensely concerned with human relations. E. Stengel's[5] studies of suicidal behaviour patterns showed that preoccupation with other people and an urge to influence and communicate with them are common to most suicidal acts. These preoccupations would have to be part of the mental state produced in the experimental group. Possibly, if this social aspect of suicidal acts had been taken into account in the psychological preparation of the experimental subjects, the notes might not have differed as they did. The question, therefore, why some people write suicide notes and others do not still remains to be answered. Perhaps the proportion of the note-writers will be found to be about the same as that of the good correspondents in the general population. The suicide note has to be viewed as only one of a variety of methods of communication in the complex patterns of suicidal behaviour.

[1] Morgenthaler, W., *Letzte Aufzeichnungen von Selbstmördern*. Berne, 1945.
[2] Schneidman, E. S., and Farberow, N. L., *Clues to Suicide*. New York, 1957.
[3] Gottschalk, L. A., and Gleser, G. C., *Brit. J. med. Psychol.*, 1960, **33**, 195.
[4] Capstick, A., *Brit. med. J.*, 1960, **1**, 1179.
[5] Stengel, E., *J. ment. Sci.*, 1960, **106**, 1388.

SPONTANEOUS DISAPPEARANCE OF GALLSTONES

Can my gallstones be swayed away? Will they go on their own accord? These are questions that a doctor commonly hears, and so it is useful from time to time to examine the evidence for spontaneous disappearance of stones. Two possible cases were reported last year from the Ochsner Clinic,[1 2] and another in 1959 by J. F. Linsman and E. Corday.[3] The number of recorded cases is now 7.

In Linsman and Corday's case ten sizable stones (as shown on cholecystography) disappeared from the gall-

bladder of a 65-year-old surgeon. This occurred over a period of four years. In Ochsner's[1] first case multiple small gallstones shown by radiography and causing attacks of pain in a pregnant woman of 27 had disappeared by the time she was operated on 10 weeks after labour. In the second case[2] a woman of 67 had multiple stones shown on cholecystogram in 1951 and 1956, but by 1959 they had disappeared without symptoms. These three cases are similar to those recorded in previous years—multiple stones up to as much as 10 mm. in diameter disappearing over a number of years with or without colic.

Though the recorded cases are few, this is probably not an uncommon phenomenon. Gallstones are very common (50 males and 153 females per 1,000 between 50 and 59 years and 217 males and 238 females per 1,000 between 80 and 89 years[4]). About half cause no symptoms, and, broadly speaking, it is only when stones become impacted in the bile ducts or the gall-bladder becomes functionless as a result of an acute or chronic inflammation that surgery is required. Stones of up to 10 mm. can in theory, and it seems in practice, pass into the duodenum, but at this size it is difficult to see how they would pass out of the gall-bladder and down the cystic duct unless the duct was of unusually large diameter or the stones were partly dissolved and reduced to 4–5 mm. Much seems to depend on the normal emptying of the gall-bladder and bile ducts. When food enters the duodenum, bile will flow through the sphincter of Oddi. With the golden bile of the ducts comes the darker and more concentrated bile which has been stored in the gall-bladder between meals. With normal filling and emptying of such a system, even after temporary dysfunction, it is reasonable to believe that biliary stones could not form. Even if they did, they would be voided while still small. Olive oil and salines —e.g., magnesium sulphate—will assist emptying, and bile salts taken by mouth will augment the general flow of bile from the liver. Thus it has long been the practice to prescribe these substances to those suffering from gallstones.

The evidence that gallstones can be dissolved is more theoretical. If a human stone is put into ox or dog bile it will dissolve owing to the action of the bile salts. In man bile salts, together with lecithin, are also responsible for keeping cholesterol dissolved, and it would be reasonable to expect that gallstones might be dissolved if bile salts are given in sufficient quantities by mouth (they are absorbed in the intestine and excreted in the bile by the liver). A. Rewbridge[5] gave bile salts and olive oil to five patients and obtained the solution and passage of stones in two cases. In an attempt to obtain greater dissolving power C. G. Johnston and F. Nakayama[6] confirmed that the addition of phospholipids to the diet potentiates the action of the bile salts. Unfortunately it also increases secretion of cholesterol from the liver, so that neither solvent is available for dissolving the stone.

Herbal infusions and other "natural" concoctions have their adherents; a diet of crushed radishes has been advocated. But there has never been a clinical trial of such substances. Certainly any effective inhibitor or solvent of gallstones must be a compound which is excreted in the bile by the liver.

PLASTIC BRONCHITIS

Plastic bronchitis is one of the more dramatic of respiratory diseases, and many pathological museums contain disintegrating bronchial casts of varying length and completeness. It is a rare condition, and only some 300 or so cases have been recorded in the world's literature. The names of Galen and Morgagni occur among the earlier references, but most instances were recorded in the nineteenth century; four cases of recurrent plastic bronchitis have recently been reviewed.[1]

The disease may occur at any age, but is commonest after 40. The attacks may be single or recurrent and may affect any part of the lungs, their special feature being the formation of tenacious mucous plugs in the bronchi which often lead to pulmonary collapse. The symptoms, which usually occur during acute or subacute bronchitis, are dyspnoea, a feeling of suffocation, discomfort behind the sternum, and sometimes a localized wheeze. Sooner or later a plug of sticky mucus is either expectorated during a fit of coughing or, if the condition is recognized, is aspirated through a bronchoscope, with almost instantaneous relief of symptoms. Rarely, extensive obstruction of the airway leads to extreme distress, and a few fatalities have been recorded.

The characteristics of the mucous plugs are unremarkable. When floated in water the bronchial branches are clearly seen and may extend from the carina down to the sixth or seventh divisions in the lung. The casts are greyish and have a smooth surface; they may contain pus cells, eosinophils, epithelial cells, bacteria, Charcot–Leyden crystals, and Curschmann's spirals. Indeed, they appear to be no more than a peculiarly viscid form of bronchial mucus. The bronchial walls usually show moderate inflammatory change.

There are many well-recognized circumstances in which the air passages are obstructed by sticky mucus. For example, the smaller bronchi are often plugged in bronchitis and asthma and the larger bronchi in measles, whooping-cough, and after an upper abdominal operation. Perhaps the two features which separate plastic bronchitis are the sudden yet unexpected symptoms and the size and length of the casts. Clearly, its existence must always be remembered as a cause of bronchial occlusion. In mild cases the inhalation of steam or trypsin, combined with postural drainage and percussion, should be sufficient to dislodge the plug. For increasing distress bronchoscopic aspiration is essential both to confirm the diagnosis and to obtain relief. Antibiotic drugs should be given to combat infection distal to the obstruction, and antispasmodics may be necessary if asthma coexists.

[1] Ochsner, S. F., *Amer. J. Surg.*, 1960, **99**, 336.
[2] —— and Giesen, A. F., *Amer. J. Roentgenol.*, 1960, **83**, 831.
[3] Linsman, J. F., and Corday, E., *J. Amer. med. Ass.*, 1959, **171**, 120.
[4] Horn, G., *Brit. med. J.*, 1956, **2**, 732.
[5] Rewbridge, A., *Surgery*, 1937, **1**, 395.
[6] Johnston, C. G., and Nakayama, F., *Arch. Surg. (Chicago)*, 1957, **75**, 436.

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SURGERY IN THE CONGO

BY

B. W. FOX, F.R.C.S., F.R.C.S.Ed., F.R.A.C.S.

Surgical Registrar, Postgraduate Medical School, Hammersmith Hospital, London; formerly Surgeon to Australian Red Cross Field Force, Congo

Under the Belgian colonial administration the medical services for the Belgian Congo were very good. However, all the doctors were Belgian and all important administrative posts were filled by Belgians, so that after their precipitate departure in July, 1960, all medical control completely collapsed.

Added to this was the outbreak of savage intertribal warfare that had previously been held in check by the Belgian colonial forces. As a result many native medical assistants and orderlies were forced to flee for their lives from their place of employment to their own hereditary tribal areas. Many of them were slaughtered by marauding tribesmen in the hospitals or *en route*. There was a lack not only of trained medical personnel but also of public health inspectors, sanitary engineers, electricians, and motor mechanics. In fact, the country was in total chaos.

Battle Casualties

My first introduction to this turmoil was in the mining town of Bakwanga, in the centre of the Congo bush-land. The Australian medical team arrived on the second day of heavy fighting between Federal Government troops and rebel soldiers of the secessionist "mining state." Both sides were armed with the latest weapons and light artillery.

Being without much equipment of our own, we made use of whatever facilities we could find and scavenge. We set up in the beleaguered native hospital of Disele and began work immediately. The hospital was formerly owned by the Forminiere Mining Company and was superbly equipped for a native workers' hospital, except that now there were no orderlies, no water, and no electricity or food.

Operations were performed under sweltering conditions in swim trunks only, with bare hands soaked in alcohol-iodine and instruments sterilized by boiling in water carried by hand from a well some 300 yards (275 metres) away. The thing that impressed me most was the fortitude of the Congolese, both civilians and soldiers, rebel and Government alike. Despite the most horrible shrapnel wounds, bullet wounds (Fig. 1), bayonet or spear wounds, and burns, they were incredibly courageous and would lie quietly on the ground awaiting their turn to be operated on. Even the smallest children (Fig. 2) rarely cried or complained. Also it must be pointed out that most procedures were carried out under local or spinal anaesthesia because we lacked sufficient general anaesthetic.

Chest wounds presented an interesting feature here. At this hospital I treated four cases of penetrating wounds of the chest—two bullet wounds, one bayonet wound, and one shrapnel injury. In none of these cases had the lung collapsed, so that it was possible to carry out a debridement of the wound and a limited exploration of the lung, and securely close the chest under local anaesthesia. The reason for this is the high incidence of pulmonary tuberculosis among the Congolese and the numerous adhesions between the visceral and parietal pleura which prevent the lung from collapsing.

All patients, and often their relatives, invariably demanded to be shown the bullets or shrapnel that had been removed. This stems from the belief of the natives that they cannot recover from a bullet wound unless the missile is removed. In many instances this was neither advisable nor expedient; consequently I collected every possible type of missile. These were kept in the operating-theatre, and by careful pre-operative interrogation we endeavoured to determine what type of

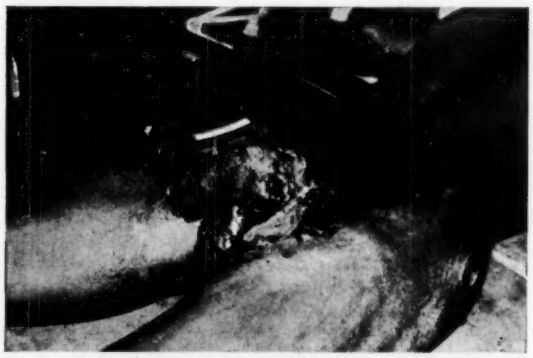


FIG. 1.—Ruptured urethra from bullet-wound during fighting at Bakwanga.

FIG. 2.—Out-patient work in a village. The child in the foreground had a supracondylar fracture of the right humerus.

weapon had inflicted the injury, and we were always able to produce a similar bullet, from those of the latest automatic weapons to the lead ball of the primitive tribesman's muzzle-loader.

One unfortunate feature of our work here was that the Government soldiers had set up their heavy mortars on the front lawn of one of our hospitals, and thus wounded civilians were afraid to approach the building for treatment as they would have to pass through these entrenchments. It was only after two days of vigorous remonstration with the local commandant that we persuaded the mortar batteries to move, and more and more wounded civilians then arrived at this hospital. As many of the civilians that we had not rescued ourselves from devastated villages did not arrive at the hospital for some four or five days after being wounded, their wounds were invariably grossly infected and covered with maggots.

A Medical Practice of 300,000 Tribesmen

After several weeks in the Bakwanga area the fighting subsided, and, accompanied by an extremely capable R.A.A.M.C. sergeant, I was sent to the small town of Luiza, on the Kasai–Katanga border some 80 miles (128 km.) from the Portuguese colony of Angola. This was the real primitive Africa—a land of tom-tom drums, large tracts of dense bush, crocodiles, and hippopotami.

Although Luiza was the administrative capital for a huge area, apart from the hospital, a small Government administrative building, and five native shops, the town merely consisted of dozens and dozens of native mud huts (Fig. 3) scattered in some 12 villages about the hospital. The population consisted of four Belgian Catholic nuns, one Italian builder, one Indian, and some 6,000 tribesmen. The nearest doctor was 200 miles (320 km.) away, and we were informed by the local Congolese administration that our hospital now provided the only doctor for a native population of 300,000 people.

The Luiza hospital was a native hospital constructed in 1954 by the Belgian administration, and had a total of 250 beds, including the medical, surgical, maternity, and tuberculosis sections. In addition this hospital maintained and administered four small rural dispensaries (out-patient clinics) at Tende, Yao, Kabaluku, and Kavueta, which were villages situated 60 to 90 miles (96 to 145 km.) in a circle around the hospital.

Before June 30, 1960 (independence of the Republic of Congo), the Luiza hospital staff consisted of: one European doctor, four trained European nurses (Catholic nuns), one Congolese *assistant médical*, one Congolese *infirmier*, 15 Congolese *aides infirmiers* (who included one *aide infirmier* at each of the four rural dispensaries), two Congolese assistant midwives, one European *agent sanitaire*, one Congolese hospital secretary, and one hospital mechanic to maintain the important diesel motor.

There was a very limited supply of drugs in the pharmacy, and the hospital diesel motor was broken and had not been running for three months. As a result there was no water or electricity supply for the hospital. The *x*-ray machine was out of order.

Several intelligent young Congolese young men were recruited and taught to administer certain drugs and how to change dressings in the wards. By enticing some orderlies away from neighbouring hospitals that had no doctor and were doing little work, the hospital staff gradually returned to almost its normal establishment. Then, with motor parts and diesel oil bought, begged, and stolen from here and there, it was eventually possible to restart the battered motor, thus ensuring a supply of water and electricity, and rapidly the Luiza hospital became a thriving concern.

Surgery at Luiza

The Luiza territory had not been devastated by the fighting that had occurred in many other parts of the country, so that the surgery done there does give an indication of the ordinary surgical problems to be encountered in the Republic of Congo. Most of the traumatic surgery seen in this region was the result of hunting accidents or machete fights after drinking-bouts in the villages. Over 400 minor surgical and obstetrical procedures were carried out in the four and a half months I was at this hospital, but these are not included in the analysis of operations given in Table I.

TABLE I.—*Analysis of* 332 *Major Surgical Operations at Luiza Hospital Between September* 23, 1960, *and February* 1, 1961

Operation for hernia	116
Laparotomy: (1) diagnostic for abdominal pain, (2) tuberculous peritonitis, (3) tuberculous glandular mass, (4) evacuation of tuberculous abscesses, (5) drainage of pelvic abscesses	28
Small-bowel resection	5
Partial resection of large bowel	1
Untwisting of volvulus of sigmoid colon	3
Total hysterectomy	16
Subtotal hysterectomy	5
Excision of cyst of Gartner's duct	1
Caesarean section	12
Enucleation of fibroids	6
Subtotal thyroidectomy	4
Skin grafts	29
Excision of masses about neck: (1) tuberculous glands, (2) chronic infection of submandibular gland, (3) parotid abscess	12
Salpingo-oophorectomy for ovarian cyst, pyosalpinx	22
" " " ruptured ectopic pregnancy	4
Manchester repair	1
Plastic operation on the hand (other than grafts)	11
Anteversion operations (Crossen–Gilliam and Baldy–Webster)	4
Appendicectomy	4
Closure and drainage of open wounds of thorax	2
Debridement and suture of other bullet wounds of limbs and face	9
Operations for compound fractures	3
" " simple fractures	19
Nephro-ureterectomy	1
Splenectomy	1
Haemorrhoidectomy	5
Excision of chronic hydrocele	7
Enucleation of eye	1

Hernia

Throughout the Congo the incidence of inguinal hernia is very high. It is usual for a surgeon in a rural hospital to perform four or five herniorrhaphies each day. 80% of the inguinal hernias occur in men of 35 to 40, and the indirect hernia is more common than the direct type. Various explanations have been advanced to explain the frequency of inguinal hernia in these people. I was not able to substantiate the view held by some surgeons there that the external and internal inguinal rings are closer together in the Congolese than in the whites, nor can the high incidence be ascribed to weak abdominal musculature, since most patients on whom I operated had very well developed abdominal muscles (Table II).

FIG. 3.—Mud huts at Luiza.

TABLE II.—*Analysis of the 116 Operations for Hernia at Luiza Hospital*

Simple hernia:			
Inguinal:	right	indirect	48
		direct	13
	left	indirect	20
		direct	20
Femoral	right femoral		—
	left ,,		3
Umbilical			2
Epigastric			1
Spiegelian			1
Lumbar (lower left lumbar)			1
Strangulated hernia:			
Inguinal	right	indirect	—
		direct	2
	left	indirect	2
		direct	2
Femoral	right femoral		—
	left ,,		1

A most significant feature, however, was that nearly all these people had some coincidental chronic abdominal condition such as cirrhosis, splenomegaly, and ascites (due to portal hypertension, chronic peritoneal tuberculosis, or nutritional deficiency). All these conditions produce an increase in the intra-abdominal pressure, and, particularly in the presence of a congenital sac, this often leads to a herniation of abdominal contents. It was quite common to open the hernial sac and be greeted by a flood of amber-coloured fluid looking suspiciously like urine, only to find that it was ascitic fluid that had not been clinically detectable. A case of lumbar hernia is illustrated (Fig. 4).

(*a*) (*b*)

FIG. 4.—Case of lumbar hernia: (*a*) before reduction; (*b*) after reduction.

Because of the high incidence of hernia and the ignorance of this primitive population many of the more bizarre complications were seen. Perhaps the following case will serve to illustrate this.

Case History.—In March, 1960, a Congolese woman aged approximately 40 experienced a sudden onset of generalized abdominal pain together with the appearance of a tender lump in the left groin. The pain persisted for several days, during which time she began to vomit and did not open her bowels. On the seventh day the swelling in the groin burst and discharged copious amounts of yellow semi-solid material. After this she felt much improved. From then on her bowels did not open and she continued to discharge this material from the opening in the groin. In May, 1960, she presented at a tiny rural dispensary and was treated by the Congolese orderly with antibiotics in the belief that she had a discharging bubo from lymphogranuloma inguinale, which is quite common in this region. When she was seen at Luiza Hospital in October, 1960, it was obvious that she had a faecal fistula, probably due to the ulceration through the skin of a strangulated femoral hernia. The patient was emaciated and could walk only with help. Laparotomy confirmed the diagnosis. The terminal ileum was incarcerated in the left femoral canal, and the small intestine above the hernia was hypertrophied but not dilated, while the bowel distal to the fistula was collapsed and did not contain faeces. After resection of the involved ileum and a femoral herniorrhaphy, the patient made a rapid recovery.

Umbilical hernia is commonly seen in the villages, although few appear to give symptoms (despite their massive size), and thus the people with this condition do not come to the hospitals for surgery. After childbirth in the villages the umbilical stump is often smeared with mud and goat dung, which produces a raw, infected umbilical region and a scarred area in the anterior abdominal wall which subsequently attenuates and results in an umbilical hernia.

Gynaecology

Operations for gynaecological problems feature high on the list of surgical work in the Congo. Neglected ovarian cysts and fibroids of immense size were exceedingly common. Many of the villagers with large ovarian cysts were convinced they were pregnant and waited for several years for babies that never arrived.

Venereal disease, particularly gonorrhoea, was very common, so that inflammation of the uterus and adnexae with its legacy of dense adhesions made operations in the pelvis rather hazardous. Since I had no facilities for cystoscopy and ureteric catheterization, in several cases I was forced to be content with a subtotal hysterectomy despite my surgical training about the risks of leaving the cervix behind.

As will be seen from Table I, caesarean section was often performed. The indication in each case was either disproportion—a small pelvis and a large baby—or a history of previous caesarean section. When it is remembered that many of the Congolese have their first child when about 15 years of age it will be realized how frequently obstructed labour can occur. Many of the women I operated on had had previous caesarean sections, and, though it is possible that some of these were performed by Congolese medical assistants or male nurses in the more remote regions without proper indications being present, nevertheless caesarean section had to be done again.

Burns and Skin Grafts

Epilepsy is not uncommon among the Congolese, and may be idiopathic or the aftermath of syphilis, encephalitis, cerebral malaria, or birth trauma. Epileptiform convulsions occurring while the native is crouching around his fire frequently result in burns. Burns of 5–6% of the surface area were commonly seen, but, fortunately, no burn larger than 10%.

The village witch-doctors were responsible for the other superficial burns we had to treat (Fig. 5). I came to know some of these "doctors" quite well and learned much about their "art." A villager complaining of pain in some region of his body may be treated

by the witch-doctor in one of two main ways. There were several other little tricks, but the following were the two most commonly encountered. Firstly, he may give his patient some dreadful corrosive concoction to swallow, but more often he prefers to apply boiling palm-oil to the skin over the painful region so that the excruciating superficial pain of the burn causes the

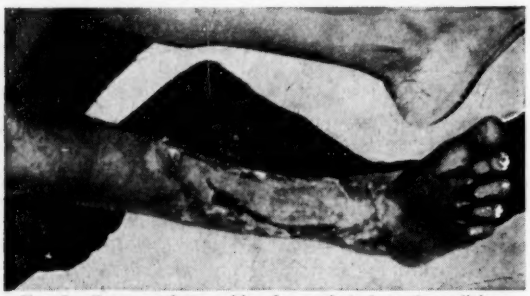


FIG. 5.—Burns on leg resulting from witch-doctor's medicine.

patient to forget his previous internal malady. The more skilled performer may make 20 to 30 tiny subcutaneous cuts about the tender area and then smear into these a tarry abrasive paste. Both these methods eventually lead to a sloughing of the skin and an angry infected raw area which it is necessary to cover by skin graft.

With half a safety-razor blade held in a Kocher forceps as a skin knife, split-skin postage-stamp grafts were used on many occasions and, surprisingly, almost invariably survived in their entirety despite the presence of pus about the site to be grafted. Plastic surgery is particularly heart-breaking among these primitive people, as they will insist on removing the bandages or just leaving the hospital after operation and making off into the jungle for five or six days, then returning and expecting continuation of their treatment. It was impossible to refuse these delightful people treatment, and often we would follow an absconder 30 to 40 miles (48–64 km.) to his village and persuade him that it was in his interest to return.

Laparotomy for Diagnosis

The Congolese are great hypochondriacs and marvellous actors, with a passionate desire to be operated on. Thus the phrase "Munganga koopanda doosama bicola" (Doctor, operate, I have terrible pain), accompanied by very realistic writhing motions and contortions, made a very convincing picture of some abdominal catastrophe even in the absence of definite physical signs. In my early days among these people, with a poor appreciation of their mentality, a limited grasp of the Tshiluba language, and the absence of any diagnostic facilities, when presented with someone in such "obvious" pain I felt obliged to perform a laparotomy despite the absence of definite physical signs. After three or four unnecessary laparotomies I became more discerning.

All forms of tuberculous involvement of the peritoneum, mesenteric glands, intestine, and even of the liver were seen. Abdominal tuberculosis was extremely common, and accounted for many of the cases of vague abdominal pain.

Anaesthesia and Resuscitation

In the absence of any general anaesthetic we were forced to do all operations under local or spinal anaesthesia. Local infiltration of the region with lignocaine was used for simple hernia, caesarean section, and operations about the head and neck.

Spinal anaesthesia was used in all other cases. For a person little versed in the art of anaesthesia I must confess that I entered upon the field of spinal anaesthetics with some trepidation. Heavy cinchocaine was used, 2.5 ml. being introduced each time, and for upper abdominal work, such as splenectomy, anaesthesia could be obtained up to T 4 level without difficulty. Spinal anaesthesia was given on more than 200 occasions without untoward complications.

In such a remote area resuscitation was quite a problem. On arrival at Luiza I determined the ABO blood groups of the hospital employees and all the prisoners in the local gaol as potential donors. There were problems, however, in that these people have an aversion to giving blood to people they do not know, and also, as a result of malaria, chronic malnutrition, etc., many of these people had a haemoglobin of 60% or less and were not suitable for use as donors. An inducement of 100 francs for 1 litre of blood did provide an adequate number of donors when the need arose.

In the case of ruptured ectopic pregnancy and haemoperitoneum the blood was scooped out of the peritoneal cavity with a sterile teacup, citrated in a bowl, strained through gauze to remove any clots, and infused back into the patient. This procedure was performed on three occasions without trouble.

In 42 blood transfusions (for medical and surgical cases), despite the fact that only ABO grouping and a thorough clinical examination of the donor were carried out, no transfusion reactions occurred.

Interesting Anomalies

Pre-auricular Sinus.—I observed eight people with pre-auricular sinus. This appears to be common in this region. In only two cases was the sinus bilateral and in only one case was I able to detect the presence of a mole immediately anterior to the sinus. One case had multiple secondary sinuses with a past history of recurrent infection, but all the other cases were symptomless.

Accessory Digits.—Another anomaly encountered there was the frequent presence of an accessory digit on the ulnar aspect of the little finger. I saw this condition in six people, and in four of them there was an accessory finger on both hands. This sixth digit usually grows from the middle phalanx of the little finger and varies in its degree of development from a rudimentary horn of several millimetres to a mature finger of one or two phalanges. There is always a nail present. The three adults I saw with this accessory digit refused amputation as they regarded it as a good-luck sign.

Conclusion

I hope that this rather discursive commentary will illustrate the types of surgical problems to be encountered in the Congo and the urgent requirement for more medical personnel in this new country.

I thank Professor Ian Aird, of the Department of Surgery, Postgraduate Medical School, Hammersmith Hospital, London, for the help he has given me in writing this article, and Professor Maurice Ewing, of the Department of Surgery, University of Melbourne, who made it possible for me to go to the Congo.

MATERNITY WORK IN A GENERAL-PRACTITIONER UNIT

BY

J. S. K. STEVENSON, M.B., Ch.B., D.Obst.R.C.O.G.

General Practitioner, Stevenston, Ayrshire

I feel that the general practitioner has a definite part to play in the obstetrics services of the future. The pattern of the present service in Ayrshire seems to be worth copying, and this paper gives an outline of the local obstetrical facilities, and, retrospectively, assesses the outcome of all the pregnancies which occurred in a two-year period in the practice run by my two partners and myself.

Services Available in the Area

Consultant Obstetric Service.—This is centred in the maternity section of Ayrshire Central Hospital, Irvine (112 beds), some seven miles from the practice centre, and provides consultant antenatal clinics, accommodation for booked and emergency cases, and antenatal relaxation classes. There is also a unit for premature babies. The hospital serves the whole of the county of Ayr. There are, in addition, nine peripheral antenatal clinics conducted each week by the registrars from the hospital.

General-practitioner Maternity Hospital Units.—There are three such hospitals in the county—one at Kilmarnock (33 beds), one in Ayr (18 beds), and Buckreddan Maternity Hospital, Kilwinning (33 beds). Buckreddan Hospital, which is used by us, is permanently staffed by a matron, State-registered midwives, and nurses, and is four miles from the practice centre. It is also used for normal confinements when the family doctors are unable to undertake their supervision because of geographical difficulties. Members of the consultant unit are available to attend such cases in the event of any emergency, and may also be consulted by a practitioner supervising his own patient in the hospital.

Queen's Nursing Service.—The services of the district nurses, acting as midwives, are available to those expectant mothers booked for confinement at home and to all mothers and babies in the post-natal period, after discharge from hospital. The service is supervised by the county public health authorities.

Laboratory Service.—The Central Laboratory, at Ayrshire Central Hospital, undertakes all laboratory investigations for the area, and provides a comprehensive service for all general practitioners.

All the above services are used by us, and with so many available the expectant mother could easily be lost in the maternity welfare maze. However, by close co-operation between hospital staff, district nurse, and family doctor, cases are satisfactorily supervised. It is fortunate that such close co-operation exists.

Work in the G.P. Unit

Ours is an industrial partnership practice in North Ayrshire, with 5,500 patients. During the period under review—April 1, 1958, to March 31, 1960—there were 250 pregnancies in the practice. All three partners were involved in the supervision of the pregnancies; 32 (12.8%) ended in abortion and 218 (87.2%) went beyond the 28th week. The terminal supervision was undertaken either by ourselves or the area specialist maternity unit staff (Table I).

TABLE I.—*Terminal Supervision of Pregnancies*

	G.P. Supervision	Specialist Supervision	Total
Confinements	121	97	218
Abortions	1	31	32

Of the 218 confinements, 121 (55.5%) were supervised by ourselves and 97 (44.5%) by the consultant service. As one would expect, in the majority of the abortions—31 (96.9%)—the patients were admitted to hospital, and only one (3.1%) was treated at home.

Maternity work in our general practice includes suitable booking for confinement and antenatal, intrapartum, and post-natal care.

Booking for Confinement

We undertake the complete care of all patients, except those regarded as unsuitable for confinement either at home or in the general-practitioner hospital. We have compiled a list of such cases, and all patients falling into this category are booked automatically for confinement in the consultant unit. The list is: (1) bad obstetric history, (2) subfertility, (3) elderly primigravida (over 35 years of age), (4) high multiparity (after fifth successful pregnancy), (5) previous caesarean section, (6) history of retained placenta, (7) pelvic contraction, (8) maternal essential hypertension, (9) maternal heart disease, (10) maternal diabetes mellitus, (11) maternal pulmonary tuberculosis, (12) unmarried mothers.

This list is not exhaustive, and other cases may be referred in early pregnancy on their merit. This is done by referral to the consultant antenatal clinic, by appointment, or to the local peripheral clinic, with a covering letter. Normally, such patients are seen twice at these clinics—at the initial visit and at the 36th week of pregnancy. The remainder of their antenatal care we undertake ourselves.

The supervision of all cases not so booked remains our responsibility, and we book them for confinement either at home or in the general-practitioner hospital unit. The patient makes her own booking by presenting our letter either to the district midwife or to the matron of the hospital.

The accuracy of early bookings and the ultimate place of confinement are shown in Table II.

TABLE II.—*Changes in Bookings*

Place of Booking	Original Booking	No Change	Change for Confinement
(A) Home	26 (11·5%)	25 (11·4%)	—
(B) G.P. unit ..	134 (61·5%)	95 (43·2%)	1 (0·5%) A to B
(C) Specialist unit ..	58 (27·0%)	58 (27·0%)	39 (17·9%) B to C
Total ..	218 (100%)	178 (81·6%)	40 (18·4%)

All normal primigravidae are booked for confinement in the G.P. unit, and are given the opportunity of attending one of the antenatal relaxation classes held at the consultant unit. These are conducted by the physiotherapist and members of the nursing staff and are available to all, irrespective of place of booking. The patient attends for one afternoon each week for six weeks.

Antenatal Care

The majority of patients, although attending the same partner throughout most of the antenatal period, are normally seen by at least two if not all three of us

during this time. It is therefore imperative that accurate records be kept. We find that the College of General Practitioners record cards are most suitable for this purpose. The reasons for antenatal examination having been explained, the onus to attend regularly is placed on the patient. Defaulters are sent postcards, and, if they still do not attend, a visit is made to the home and the patient asked to come to the surgery for examination.

Our aim is to make 12–14 antenatal examinations of the normal patient. For the 218 patients confined, 1,974 antenatal examinations were made—an average of nine per patient. One patient received no antenatal care, and another, whose case was complicated by essential hypertension, had 44 examinations before ultimate admission to hospital.

Blood.—At the initial visit the patient's blood is taken for grouping, haemoglobin, and Wassermann reaction. We believe it is important to know the patient's blood group early in the pregnancy, in the event of the pregnancy aborting and the patient requiring either admission to hospital or the services of the flying squad during hours when laboratory facilities are not available. Twenty-nine (11.6%) of the series were rhesus-negative. One developed antibodies during the pregnancy, her second, and the baby required a replacement transfusion.

Urine.—During the antenatal supervision the urine was examined routinely for glucose at the initial examination only. Since then an atypical case of diabetes mellitus, developing rapidly during pregnancy, was missed because the urine was not re-examined for glucose until the patient was admitted to hospital because of the intrauterine death of the foetus. It seems that regular examination of the urine for albumin in the absence of excessive gain in weight, peripheral oedema, and relative hypertension is unnecessary, while a repeat examination for glucose in the later weeks of the pregnancy may be a valuable single observation if the test were positive. Albuminuria appeared once in our series, and then only in a patient with established pre-eclamptic toxaemia after admission to hospital.

Pre-eclamptic Toxaemia

In our area there is a high incidence of pre-eclampsia. Of 6,704 births in the county of Ayr in 1959, 737 (11%) required admission to hospital in the specialist unit on account of toxaemia (Registrars Annual Report of the Registrar-General for Scotland, 1959 — Maternity Section, Ayrshire Central Hospital). Supervision of toxaemic patients involves us in more work than all other antenatal abnormalities put together, and the treatment of pre-eclamptic toxaemia in its early stages is the most important aspect of this work.

In general, if we find a gain in weight in excess of 4 lb. (1,815 g.) in a four-week period during the second and third trimester, we institute a prophylactic regime of low-carbohydrate and low-salt diet, with a reduced fluid intake and increased rest. Neither diuretics nor hypotensive agents are used. If the incipient pre-eclamptic patient is not controlled by these simple measures she is confined to bed and visited each day at home. If matters do not improve, admission to hospital is requested. Much importance is therefore attached to recording the patient's weight at each antenatal visit. An excessive gain would appear to be the most sensitive indication of the early onset of pre-eclampsia—relative hypertension, overt oedema, and, in particular, albuminuria developing later.

Of the 218 pregnancies in our series, no fewer than 102 (46.8%) showed an excessive gain in weight at some point in the antenatal period. Twenty-four (11%) of our patients were admitted to hospital on account of toxaemia ; 17 of these cases were pure pre-eclampsia and 7 were complicated by essential hypertension. (The percentage is exactly the same as for the county as a whole in the year 1959.) We feel, however, that with careful supervision the severity of the toxaemia can be lessened, and the likelihood of a more mature foetus can be increased. To illustrate this, details of the 17 cases of pure pre-eclamptic toxaemia are given in Table III. The foetal mortality rate was nil.

TABLE III.—*Babies' Weights in Cases of Pre-eclamptic Toxaemia Requiring Admission to Hospital*

No.	Age	Parity	Week of Onset of Pre-eclampsia	Week of Hospital Admission	Baby's Birth Weight	
					lb. oz.	g.
1	19	Prim.	31st	39th	6 4½	2,855
2	18	0 plus 1	28th	39th	6 12	3,060
3	21	Prim.	29th	34th	*4 11	2,126
				(twin preg.)	*3 14½	1,770
4	21	1 plus 0	25th	At term	9 9	4,335
5	23	Prim.	34th	,, ,,	7 2½	3,255
6	34	1 plus 0	34th	39th	7 5	3,315
7	36	2 ,, 1	23rd	At term	10 1½	4,585
8	34	1 ,, 0	33rd	39th	8 7½	3,850
9	27	1 ,, 0	38th	38th	6 8½	2,960
10	26	Prim.	39th	39th	7 7½	3,395
11	38	3 plus 0	34th	38th	9 12½	4,445
12	30	Prim.	24th	39th	7 0	3,175
13	21	1 plus 0	34th	36th	7 3½	3,275
14	19	Prim.	30th	37th	7 2½	3,255
15	24	2 plus 0	33rd	39th	7 8½	3,415
16	29	3 ,, 1	36th	39th	6 11	3,035
17	26	Prim.	31st	38th	7 8¾	3,425

* Premature.

Intrapartum Care

Cases suitable for home confinement are carefully chosen and usually present no difficulty. These are attended by the district midwife and a student midwife on district from the training school at the specialist unit. Despite the expected normality of home deliveries, we attempt to be present at all of these.

Of the 25 patients confined at home, 24 were normal and one had a spontaneous breech delivery. The breech presentation was not diagnosed in the antenatal period. One of us was present during the second and third stages of 18 of the confinements, and performed the actual delivery of nine of them. None of us was present during the second and third stages of seven of the cases, but these were usually seen by one of us during the first stage.

One case was complicated by a retained placenta and required the services of the flying squad. There was no history of retained placenta. (This was the only call made on the flying squad during the series.) The placenta was removed manually in the patient's home.

Cases Confined in the G.P. Unit

These were our responsibility, and one of us was normally present during the first stage. Of the 96 confinements in the unit, one of us was present during the second and third stages of 61, delivering 40 of these. The remaining 35 confinements were supervised in the second and third stages by the duty midwives. The partner on duty for emergencies during any particular day undertakes any confinement during his spell on call. Any other system would be of no benefit to the patient, and would certainly curtail our free time.

The hospital is equipped to deal with most emergencies, and we are able to undertake minor obstetric operative procedures when the need arises. By arrangement with the hospital consultants, we also perform surgical inductions of labour for post-maturity, on the understanding that if the patient does not go into labour within 24 hours she will be transferred from the general-practitioner unit to the consultant unit. Because of lack of sterile conditions surgical induction is never attempted in the patient's home.

Of the 96 cases confined in the G.P. unit, 95 were booked and one was referred from home for surgical induction on account of post-maturity.

Normal Deliveries.—Of the 96 confinements, 92 were normal deliveries, 8 of these after mediolateral episiotomy, all sutured in two layers by one of us. Two sets of twins were delivered, all four deliveries being normal. Multiple pregnancy was diagnosed in one of the cases, but the patient refused admission to the specialist unit. The diagnosis was not made in the other case.

Forceps Deliveries.—Four cases were delivered by low cavity forceps, after episiotomy. Pudendal block local anaesthesia was used in all four. High and mid-cavity forceps deliveries were not attempted.

Surgical Induction.—Seven cases of post-maturity were induced surgically. Six proceeded to have normal deliveries. One failed to go into labour within 24 hours and was transferred to the consultant unit, where she delivered herself normally with the aid of an intravenous "syntocinon" (synthetic oxytocin) drip.

Post-partum Haemorrhage.—Our routine is to give ergometrine 0.5 mg. intramuscularly with the crowning of the head. Two cases of post-partum haemorrhage occurred after otherwise normal deliveries. One patient collapsed and required transfusion with plasma before manual exploration of the uterus was made under general anaesthesia. The other did not require initial transfusion, but in view of her anaemic state (Hb 40%) was given 2 pints (1,140 ml.) of whole blood by one of us on the following day.

Retained Placenta.—This complication occurred twice in the 96 cases. On both occasions manual removal of the placenta was carried out by one of us. The general anaesthetics were administered by a member of the consultant unit.

Foetal Mortality.—There were no stillbirths among the babies delivered at home and in the G.P. unit. One child delivered in the latter lived for only an hour. Post-mortem examination revealed renal agenesis.

Cases Confined in the Consultant Unit

The intrapartum management of the cases booked for or referred as emergencies to the consultant unit is undertaken wholly by the staff of the unit. Ninety-seven of our confinements took place in the consultant unit: 58 cases were booked in early pregnancy and 39 were referred on account of abnormalities developing. Particulars of the 97 cases are given in Tables IV and V. A comparison of the numbers and types of delivery under G.P. and specialist supervision is shown in Table VI (of the deliveries listed as breech, 10 were failed external versions).

Perinatal Mortality.—The perinatal mortality for the series was 9 (4.2%). The greatest risk to the foetus would appear to be associated with maternal essential hypertension. Among the seven cases booked for confinement in the specialist unit, only three babies survived. There were two stillbirths, one of which was premature, and two babies died in the early neonatal period; again one was premature. One foetal loss was caused by accidental haemorrhage associated with hypofibrinogenaemia in the mother, and one, previously mentioned, was due to renal agenesis. The remaining three babies were premature. None of the foetal losses was thought to be preventable.

TABLE IV.—58 *Cases Booked for Confinement in Consultant Unit, with Outcome of Confinement*

Reasons for Booking	No.	Type of Delivery	Perinatal Mortality
Healed, maternal pulmonary tuberculosis	12	11 normal, 1 forceps	Nil
For sterilization	8	6 normal, 1 forceps, 1 breech	,,
Essential hypertension	7	6 normal, 1 breech	4
Bad obstetric history	7	6 ,, 1 section	1
Social reasons	7	7 ,,	Nil
Maternal heart disease	3	3 ,,	,,
Unmarried mothers	3	1 ,, 1 breech, 1 forceps	,,
Previous caesarean section	1	1 repeat section	,,
Elderly primigravida	1	1 normal	,,
Grand multipara	1	1 breech	,,
Pelvic contraction	1	1 Normal	1
History—retained placenta	1	1 ,, (repeat manual removal of placenta)	Nil
Others (including twins booked for social reasons)	6	4 normal, 1 forceps, 1 breech	,,

TABLE V.—39 *Cases Referred to the Consultant Unit, with Outcome of Confinement*

Reasons for Referral	No.	Type of Delivery	Perinatal Mortality
Pre-eclamptic toxaemia	17	13 normal, 1 breech, 2 forceps, 1 section	Nil
Antepartum haemorrhage	6	4 normal, 2 forceps	,,
Premature labour	4	3 ,, 1 breech	1
Breech presentation	3	3 breech	Nil
Intrauterine death	1	1 normal	1
Others	8	6 ,, 1 forceps, 1 section	Nil

TABLE VI.—*Types of Deliveries Under G.P. and Specialist Supervision*

Type of Delivery	Total	G.P. Service	Specialist Service
Normal	190 (87·1%)	116 (53·2%)	74 (33·9%)
Breech	11 (5·1%)	1 (0·5%)	10 (4·6%)
Forceps	13 (6·0%)	4 (1·8%)	9 (4·2%)
Caesarean section	4 (1·8%)	Nil	4 (1·8%)
Total	218 (100%)	121 (55·5%)	97 (44·5%)

Maternal Mortality.—There were no maternal deaths.

Post-natal Care.—Patients are visited daily during their stay in the G.P. unit (eight days) and daily for the first week if delivered at home. Thereafter visits are made at the discretion of the partner looking after the case. In the G.P. unit, facilities are available for the investigation of any case of puerperal pyrexia, and questions of antibiotic sensitivity may be referred to the central laboratory when either urinary or pelvic infection is suspected. The area consultant paediatrician may be requested to see any ill baby should such a consultation be indicated.

Abortions.—It is our policy to refer all abortions to the consultant unit. Ergometrine 0.5 mg. is given routinely, and morphine ¼ gr. (16 mg.), if necessary, before transporting the patient to hospital. In view of the probability of general anaesthesia being required, the patient is instructed not to take anything further in the way of food or drink. Of the 32 abortions in

the series, three were missed, two were complete, and 27 were either inevitable or incomplete. Thirty-one of these cases were admitted to the consultant unit for evacuation of the uterus, and one, in which it was obviously complete, was allowed to remain at home. Of the admissions to hospital, 30 required evacuation of the uterus under general anaesthesia.

Discussion

It is recommended in the Report of the Maternity Services Committee of 1959 (para. 70) that sufficient hospital maternity beds be provided to enable a national average of 70% of all confinements to take place in hospital. It is also recommended (para. 258) that any extra lying-in beds required should, where possible, be general-practitioner beds. This happy state of affairs at present exists in Ayrshire.

Of the 6,704 births in Ayrshire in 1959, 5,402 (80.6%) took place in hospital (Annual Report of the Registrar-General for Scotland, 1959—Maternity Section, Ayrshire Central Hospital). Of the hospital confinements, 2,648 (49%) took place in the maternity section of Ayrshire Central Hospital, and the remaining 2,754 (51%) in hospitals to which, although remaining under the overall responsibility of the area consultant obstetrician, general practitioners had access.

The object of this paper is to assess the part which can be played by the general-practitioner obstetrician practising under favourable conditions. I believe that the most essential factor in the production of such conditions is mutual trust and co-operation between the general practitioner and the members of the hospital unit with which he is dealing. This, unfortunately, is not always obtainable. In densely populated areas, where there is more than one specialist unit receiving cases, the desirable personal contact between practitioner and consultant becomes more difficult. This, however, may be compensated for in future planning by the fact that, whereas in this area some practitioners are unable to make full use of all the facilities because their practices are situated too far from the general-practitioner maternity hospitals, city practitioners would not encounter this particular difficulty.

In our area the consultants co-operate by never refusing the admission of a patient to the specialist unit. Indeed, since the consultant hospital was opened some fifteen years ago no patient has ever been refused admission because of lack of accommodation. This is made possible by the transference of normal cases in the early post-natal period—often within the first 24 hours—to one of the general-practitioner hospitals; or, in some cases, to the early dismissal of healthy patients and babies to their homes and the care of their family doctor. I believe that a normal stay of ten days in hospital after delivery, as suggested in the Cranbrook Report (para. 81), should, in the light of present circumstances, be reduced to a maximum of eight days for the uncomplicated case. The practitioner, in turn, should co-operate by providing good antenatal supervision. It should be within the scope of every general practitioner who accepts the responsibility for maternity work to provide complete antenatal supervision for the normal patient. Any omission on his part, however trivial apparently, automatically makes his antenatal supervision inferior to that provided by his specialist colleague. The general practitioner should also have a clear picture in mind of what is expected of him. He should not hold on to any patient who may progress beyond his capabilities, and, by depriving her of specialist supervision in hosptial, jeopardize her chance of a successful confinement. Even with favourable conditions at our disposal, we, in our practice, considered that we were competent to deal with only 55.5% of our confinements during a two-year period.

Another recommendation of the Cranbrook Report (para. 151) is that an appointments system should be instituted at all antenatal clinics. It may be of interest to note that this was unsuccessfully tried for a period in our practice. The failure lay with the patients in that they did not keep the appointments. This may be explained by the fact that the lives of most of our patients are governed by shift work, which tends to have an unsettling influence. They seem to prefer to await their turn during general surgery hours. From our point of view, it is refreshing to see a few healthy non-complaining patients during a routine surgery, but we nevertheless realize the advantages of the special antenatal clinic, and may consider reintroducing this with an appointments system.

Summary

An account is given of the maternity services available in Ayrshire in general, and in particular of the 250 pregnancies occurring in one North Ayrshire practice.

It is felt that many of the recommendations made in the Cranbrook Report are already in operation and available to the majority of general practitioners in Ayrshire.

I am indebted to Dr. Richard de Soldenhoff for his help and useful criticism; to the members of his staff, both medical and secretarial, at the maternity section of Ayrshire Central Hospital; to Miss Dunlop and her staff at Buckreddan Maternity Hospital, Kilwinning; to the local district nurses; to Miss D. H. McKenzie and Miss E. Houliston, for help with record-keeping; and especially to my senior partners, Dr. Lachlan Carmichael and Dr. Fraser Ross, for their constant encouragement and for carrying out two-thirds of the work described.

QUEEN OPENS BUILDINGS AT BART'S

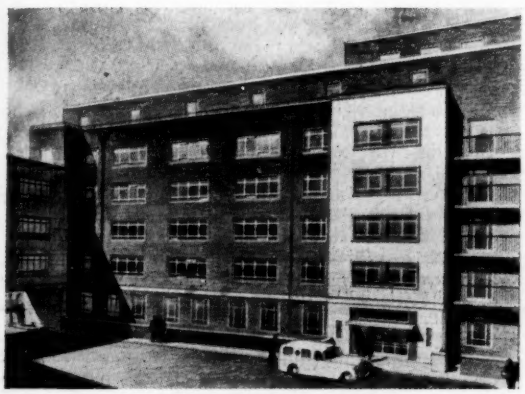
H.M. the Queen visited the Royal Hospital of Saint Bartholomew, London, on May 30 to open three new buildings which form the most substantial additions to the hospital since the King George V Block of medical wards was completed in 1935. The Queen, who was welcomed in the Great Hall by the president of the hospital, the Duke of Gloucester, formally declared open the special department ward block (to be known as the Queen Elizabeth II Wing), the Department of Radiotherapy, and the new extension to the nurses' home, Gloucester House. She was thanked by the past treasurer of the hospital, Sir George Aylwen.

The new buildings are the outcome of plans made after the war to accommodate the special department wards which had been moved to Hill End Hospital at St. Albans when war broke out and which could not be returned to St. Bartholomew's after the war because there was no room for them. The plans were for a new ward block to house 120 special department patients, and an extension to the nurses' home to house the additional nurses that would be needed. These two

buildings have been completed and are occupied. The first stage of the third building that was planned, a department of radiotherapy, has been completed. All three buildings are in Bartholomew Close. The cost of the land and of erecting and equipping the buildings —a sum in the region of £1¼m.—has been met by the hospital's endowment moneys.

Queen Elizabeth II Wing

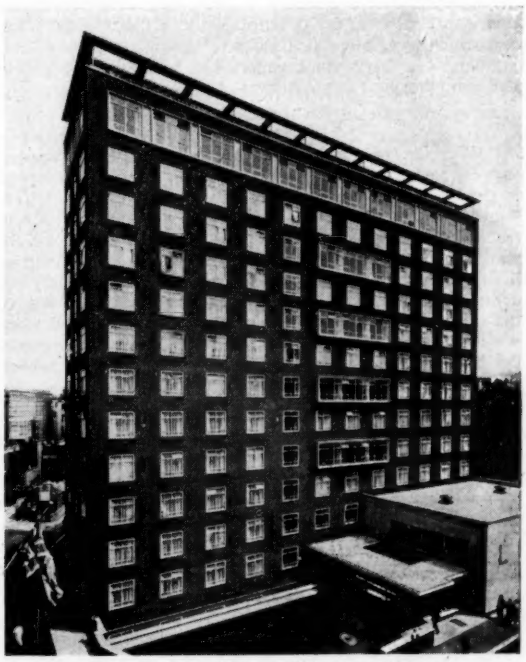
The Queen Elizabeth II Wing has five floors and a basement. The basement houses the cardiological department and a new boiler-house which will provide heating and steam services for the whole hospital. The ground floor holds the administrative offices, a diagnostic radiography department, and an isotope department. On the first, second, third, and fourth floors are the ward units with 30 beds in each, arranged in small wards. On the first floor is a ward for ophthalmic patients which has its own operating theatre adjoining. The other units house neurosurgical, ear-nose-and-throat, and thoracic patients. The fifth floor houses twin operating theatres with a theatre for radiography, a kitchen, and ancillary offices.



The Queen Elizabeth II Wing.

Radiotherapy Unit

The new radiotherapy unit has been designed to house the 15-million-volt linear accelerator unit which the hospital purchased in 1954, and which was accommodated in the Medical College in Charterhouse Square, where much experimental and research work was carried out. It is now being used for clinical purposes, together with a cobalt-60 unit. The greater part of the building lies below ground, the linear accelerator chamber being 33 feet below with one wall 10 feet thick to guard against radiation hazards. The building as it is at the moment represents



The new nurses' home, Gloucester House.

The Queen, accompanied by the Duke of Gloucester and the Minister of Health, Mr. Enoch Powell, walks from the Queen Elizabeth II Wing to Gloucester House.

stage 1 of a plan for providing a comprehensive radiotherapy department, and work on the second stage has now begun.

Extension of the Nurses' Home

As the hospital lies in the heart of the City facilities for recreation are very poor, and the new nurses' home has been planned accordingly. It is a 12-story building with bedrooms for 161 nurses, and sitting-rooms. On the lower ground floor is a 57-foot by 30-foot swimming-pool which may be used by medical students. On the same floor are automatic washing machines and spin driers where the nurses may do their personal laundry if they wish. On the eleventh floor is a nurses' training unit, with two lecture rooms, a classroom for practical work, a library, and other departments. Above this, with a magnificent view over London, is a large sun lounge. The building is linked to the main hospital by a subway.

Return to the City

"With the opening of the special department wards," says Sir James Paterson Ross, P.P.R.C.S., consulting surgeon to the hospital, in the brochure issued to mark the occasion, "the college will now be able to integrate more effectively teaching in these vital specialities, and the return of the staff to the city will facilitate the exchange of knowledge and experience. . . . Advances in medicine and surgery are continuous: the college and hospital realize their mutual dependence and responsibility for providing the soil upon which may grow to maturity the seeds sown by so many centuries of scholarship and service in the fight against disease."

The architects were Messrs. Adams, Holden, and Pearson, and we are indebted to them and to the hospital for permission to publish the drawing of the Queen Elizabeth II Wing. The other photographs are published by courtesy of Barratt's Photo Press.

Nova et Vetera

BELFAST CHARITABLE SOCIETY

Dr. Strain's book* is an interesting contribution to socio-medical history, although the copious extracts from minute-books will chiefly be appreciated by the citizens of Belfast. This story epitomizes the philanthropic work carried out by the Belfast Charitable Society from 1752 until 1948. To-day the society provides a home for 144 aged men and women of Belfast in the original Georgian building, Clifton House.

Originally established to provide a poorhouse and hospital for the employment of idle beggars and for the reception of infirm and diseased poor, the society went on to educate and support a number of poor children; to give out-patient treatment and domiciliary medical and nursing care; to employ leading Belfast practitioners on its medical staff, including at a later date Sir William Whitla; to provide for the treatment of infectious diseases; to make industry go hand in hand with charity; and to cope with famine, typhus, and cholera. It also, after a long, bitter, and involved struggle, helped to secure a permanent and adequate water-supply for Belfast.

The book is well produced. There are a few misprints: for instance, on the portrait page facing p. 305 the third Marquess of Donegall is stated to have died in 1833 instead of 1883.

ARTHUR S. MACNALTY.

*_Belfast and Its Charitable Society. A Story of Urban Social Development._ By R. W. M. Strain. (Pp. 333+xvi; illustrated. 45s.) London, New York, Toronto: Oxford University Press. 1961.

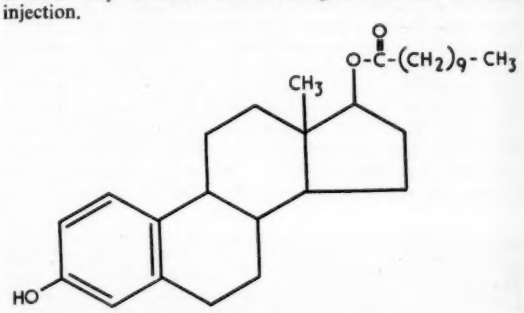
To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Oestradiol undecylenate

"Primogyn-Depot" (Schering A.G.).

Composition.—Primogen is a substituted natural oestrogen formed by the esterification of the natural follicular hormone with undecylenic acid. The depot substance consists of 100 mg. oestradiol-17-undecylenate in 1 ml. of a clear oily solution and is designed for intramuscular injection.



Pharmacology.—The action of the preparation is stated to rely on the delayed release of oestradiol, and subsequently depends on the oestrogenic properties of the latter. Oestradiol undecylenate may appeal particularly to those who favour the employment of natural as opposed to synthetic oestrogens on the grounds that they present less difficulty in their subsequent metabolism. Nevertheless it seems likely by analogy with the fate of a similar substituted natural oestrogen (phosphorylated oestradiol) that a proportion of the released oestrogen becomes protein-bound and concentrated in the liver and reticulo-endothelial system. Much of the remainder is doubtless rapidly excreted in conjugated form in the urine.

Therapy.—Primogyn-depot is advocated for the treatment of prostatic cancer on the assumption that a protracted and sustained release of oestradiol takes place after intermittent intramuscular injection. It is suggested that the depot action remains demonstrable for 4–6 weeks, though for the maintenance of an even level of hormone injections at approximately three-weekly intervals are required. While depot therapy offers certain advantages in relieving the tedium of oral administration, the inconvenience of repeated injections and possible inconstancy of the rate of release of the hormone have to be considered. As to the latter, the manufacturers claim that an intensive oestrogenic effect can be achieved and an adequate level of hormone maintained by intramuscular injection of one ampoule (100 mg.) every three weeks. If necessary, dosage can be increased by doubling the dose or shortening the period between injections.

Side-effects.—Clinical trials suggest that tolerance is good and local or general side-effects on metabolism or the circulation need not be feared. There has been no indication that liver function is affected.

Contraindications.—By analogy with the metabolic effects of large doses of other oestrogenic compounds administered parenterally, caution should at present be observed in cases with hepatic disease and those suffering from cardiac insufficiency with oedema.

N.H.S. Basic Price.—Ampoules, 10 mg., 1 for 7s. 1d.; 100 mg., 1 for 17s. 4d.

The *Revue Internationale de la Croix Rouge* is now published in an English edition.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Phenindione and Blood-coagulation Factors

SIR,—Mr. K. W. Denson in his interesting article (April 29, p. 1205) raises several questions concerning the importance of Christmas factor (factor IX) during anticoagulant therapy.

Significance of Christmas Factor for the Bleeding Tendency

His lowest recorded value of 21% of this factor during such therapy is definitely above the critical level for haemorrhage. This result, therefore, could invite the clinicians to disregard the Christmas factor as a cause of bleeding complications and, consequently, to prefer the one-stage prothrombin time for the control. I believe that these conclusions are misleading and potentially dangerous for the following reasons:

(1) Several authors have reported instances of bleeding complications without local predisposing cause in patients with a Quick's prothrombin time within the accepted therapeutic range. Most workers seem to agree with the conclusion of Hunter and Walker[1]: "There is, therefore, beyond certain limits no hard-and-fast correlation between the results of the Quick test and the tendency to bleed." Why is this so?

(2) The one-stage test of Quick gives a measure of the combined effect of prothrombin, factor VII, and factor X (Stuart–Prower factor). Severe depressions of one of these factors, giving rise to spontaneous haemorrhage, regularly prolong the prothrombin time above the therapeutic range, provided the thromboplastin preparation is sufficiently sensitive to depressions of factor VII and factor X. This conclusion is supported by the fact that the prothrombin time is prolonged beyond the therapeutic range in congenital deficiencies of one of these factors which are severe enough to give rise to *spontaneous* bleedings.

(3) The haemorrhagic syndrome caused by overdosage of anticoagulants resembles that seen in haemophilia and Christmas disease. Even haemarthroses have been observed.[2–6] On the other hand, spontaneous haematuria has very seldom been observed in congenital factor-VII deficiency and in factor-X deficiency only associated with other severe bleeding manifestations.

(4) The bleeding tendency during anticoagulant therapy as measured by the secondary bleeding-time test parallels the Christmas-factor deficiency in a manner similar to the results of transfusion experiments in Christmas disease.[7] It is independent of the levels of factor VII. So far, we have insufficient data regarding a possible correlation also between the secondary bleeding-time and the level of factor X. Factor X, however, is reflected in the Quick's test. The secondary bleeding-time becomes progressively prolonged both in Christmas disease and during anticoagulant therapy, with consequent defective haemostasis, whenever the Christmas factor is depressed below 15%. The risk of bleeding increases rapidly with decreasing values below 10%. The *clinical* problem, therefore, is this: Does anticoagulant therapy depress the Christmas factor below the 10% level? Can such depressions occur when the prothrombin time is still within the so-called "therapeutic range"?

(5) Depression of Christmas factor below the haemorrhagic level of 10% has been reported from many laboratories since Biggs and co-workers[8] suggested that its level in the blood was reduced by coumarin drugs. Johnson *et al.*[9] gave the indandione drug "hedulin" (phenindione) to 10 patients in dosages to prolong the prothrombin time to 53 seconds. The Christmas-factor levels fell to zero. (Technique: Johnson and Seegers.[10]) Our own findings in patients on long-term therapy are more similar to Mr. Denson's results, but many of our values are between 10 and 20%, and we have repeatedly recorded values below 10%. There seems to be no doubt, therefore, that Christmas factor can be reduced below the critical level. We have not sufficient data for calculating the exact frequency of such situations, because bleeding episodes have become very rare. Bachmann, Duckert, and Koller[11] by systematic investigations for one year on patients with bleeding under "marcoumar" (phenprocoumon) therapy found that "about *one-fourth* of these bleeding patients had very markedly decreased factor IX levels (2–10%) with Stuart–Prower factor levels higher than 10% and Quick values in the therapeutic range."

From both clinical and experimental evidence, therefore, it must be concluded that bleeding *can* occur because of severe reduction of Christmas factor, and this was one of the reasons for developing the thrombotest method. The other and not less important reason was to devise a simple and still reliable test which would allow decentralization of anticoagulant therapy.

There are two possible reasons why Mr. Denson has not observed patients with Christmas-factor concentrations at low levels. Firstly, a small number of patients only have been examined. Secondly, the method applied may give too high values. He applied the thromboplastin-generation test of Biggs and Douglas,[12] modified by the addition to the incubation mixture of an "eluate of Prower–Stuart factor." We appreciate the thromboplastin-generation technique as an excellent qualitative diagnostic test and a useful research tool for specific purposes, but our experience has convinced us that this principle has serious drawbacks as a quantitative assay.

Firstly, *serum* is best avoided in quantitative assay techniques for the intrinsic clotting system, because it contains varying amounts of residual clotting factors (also prothrombin which gives rise to thrombin during incubation) and intermediates or "activation products." The activities recorded, therefore, do not allow reliable deductions concerning the original concentration of a specified clotting factor in *plasma*. This is especially true for the quantitation of the Christmas factor, because the activity of this factor is extremely sensitive to the presence of intermediate products. Secondly, what is left of activities in the incubation mixture after 12 minutes depends not only on production, but also on the rate of inactivation of "blood thromboplastin" and thrombin, processes which are uncontrollable. I presume that the Stuart–Prower factor eluate applied has been tested and found to be without any corrective effect on plasma or blood from patients with Christmas disease.

Sensitivity of the Thrombotest to Christmas Factor

With regard to this point, Mr. Denson states: "Evidence will be presented in a further publication to demonstrate the almost complete insensitivity of the reagent to Christmas-factor deficiencies." "Such reliance upon a false sensitivity, however, may be misleading or even hazardous when it is realized that a plasma sample having a Christmas assay of less than 1% may show a value of between 50 and 80% by the thrombotest method."

Unfortunately, Mr. Denson seems to have missed the essential point in this connexion, namely—that thrombotest has been devised for the control of anticoagulant therapy and not as a test for disclosing Christmas disease. The important point is to have a test which is sensitive to Christmas factor and which may herald a risk of bleeding complications in patients under anticoagulant therapy at *therapeutic levels*. For thrombo-

test, we have assessed the optimal therapeutic level to 15% and the lowest safe level to 10%. If Quick's original method with rabbit-brain thromboplastin is used and the therapeutic level is assessed to 2–2½ times normal, this will roughly correspond to 7 to 12% with the thrombotest method. The pertinent question, therefore, is: What is the sensitivity of thrombotest at *these* levels? Everyone can answer this question correctly by doing the following simple test: Normal citrated plasma and citrated Christmas-disease plasma are both diluted as follows: 0.6 ml. of plasma (which corresponds to 1 ml. of citrated blood) is added to 9.4 ml. citrated saline. Thrombotest is then performed by the standard technique for citrated whole blood. The difference in clotting times gives a measure of the sensitivity to Christmas factor at the 10% level of the other factors. This difference is usually 40 to 50 seconds, a finding which demonstrates a good sensitivity towards the intrinsic clotting system, being of the same order as the sensitivity to factor VII of the extrinsic system. For this experiment it must be controlled that prothrombin, factor VII, and factor X are identical in the two plasmas. Christmas-disease plasma often has a subnormal concentration of factor VII. If this is the case, the normal plasma must be adjusted to the same concentration of factor VII as the Christmas-disease plasma by mixing it with the appropriate amount of factor-VII-deficient plasma. It is further very important that all plasmas are collected by silicone technique.

Probably the best way to assess the merits of a test is to submit it to extensive clinical trials. The thrombotest has now been used for the control of thousands of patients in several countries. At our out-patient control laboratory about 2,000 patients have been controlled by this test for the last two years. Bleedings without local cause have not been observed in this material as long as the thrombotest values have been above 10%.

Details on the levels of clotting factors during anticoagulant therapy will be reported in a forthcoming paper.—I am, etc.,

Institute for Thrombosis Research, University of Oslo. P. A. OWREN.

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Intubated Jejunostomy

SIR,—May I say how much the paper on "Intubated Jejunostomy for Recurrent Small-bowel Obstruction" by Mr. R. J. Luck and Mr. H. H. G. Eastcott (April 29, p. 1200) has been appreciated? It is indeed a life-saving measure, and I have intubated in this way seven patients during the last ten years, all of whom made an unexpected and uneventful recovery. The patients in every case were elderly, admitted in the late stages of peritonitis or obstruction due to malignant disease, and in whom it was almost impracticable to replace the distended gut within the abdomen.

I well remember my first patient who had a plastic peritonitis with faecal contamination, having been treated by his local doctor by repeated paracentesis abdomini for ten days until the practitioner extracted faeces through his needle. At laparotomy the patient's gut was in such a tangled mass that it was intubated through the terminal ileum upwards and the tube brought out through a jejunostomy in the left subcostal region. The tube was then connected to continuous suction and the abdomen closed. The very act of opening the gut decompressed it, with the aid of a sucker, and so allowed the abdominal contents to be replaced and the wound closed. Forty-eight hours later bowel sounds had returned and the patient made an uneventful recovery.

This same story has been repeated each time with equal success, and, although Mr. Luck and Mr. Eastcott described their intubation for recurrent small-bowel obstruction, it is well to remember that it can be a life-saving method in the initial management of paralytic ileus, whether it be of infective, toxic, or of reflex aetiology.

My most recent case was a lady of 54 who had a carcinoma of her pelvic colon involving two separate areas of small intestine and urinary bladder. Her colon and two pieces of small intestine were resected together with a portion of the bladder. The small intestine was intubated retrogradely from the terminal ileum to the upper jejunum as described, and within 48 hours bowel sounds had returned and the patient has made an uninterrupted recovery. A very poor prognosis was envisaged when this patient was first seen. The histology report, however, has shown adenocarcinoma in all the structures removed, but no glandular metastases, nor were there any hepatic metastases at operation. It would appear, therefore, that this patient has been macroscopically cured of her malignant disease, and what seemed at first to be an impossible task I am sure was greatly benefited by the intubation of the small gut.

The use of the Miller–Abbott tube is open to discussion because one is limited by the suction holes being in the terminal part, and I have found it preferable to use a tube of similar bore and length but in which holes can be punched at different levels, and thereby maintain a more generalized decompression of the whole of the small intestine and not be confined to that segment of the gut in which the Miller–Abbott metal end is situated. Not only is intestinal compression adequately maintained, but the mechanical action of the tube within the gut may have an irritant effect, stimulating peristalsis to recur, perhaps more readily.—I am, etc.,

London W.1. F. AUSTIN HENLEY.

Cataract and Steroids

SIR,—We read with interest your annotation (January 14, p. 116) on the occurrence of posterior subcapsular lens opacities reported by Black *et al.*[1] in patients receiving high steroid dosage for long periods. Since their report appeared we have examined by ophthalmoscopy and slit-lamp microscopy a comparable number of patients (67) who have received prednisolone or equivalent analogue in a daily dose of more than 10 mg. for more than one year.

So far we have discovered cataract in only one case, a female of 63 with rheumatoid arthritis, who had been

on steroid therapy since 1952, and who has now developed bilateral subcapsular lens opacities. Lens opacities had not been noted when she was seen by an ophthalmic surgeon three years ago, but it is of interest that this lady has received steroids in higher dosage and for a longer period than any other patient in our group. Thus, while it is very difficult to distinguish these opacities from the common senile cataract developing at this site, steroid therapy must be considered a possible causative factor in patients receiving prolonged steroid therapy in high dosage, although, to judge from our group, the risk is small.

So, although such a posterior subcapsular lens opacity does cause a disproportionate degree of visual loss, it is an extremely rare complication.—We are, etc.,

F. DUDLEY HART.
T. A. CASEY.
M. D. O'RIORDAN.

Westminster Hospital,
London S.W.1.

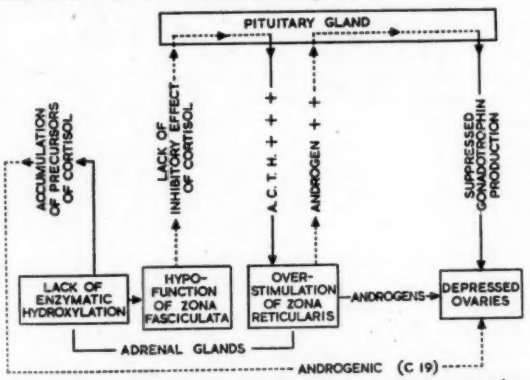
REFERENCE

1 Black, R. L., Ogelsby, R. B., von Sallman, L., and Bunim, J. J., *J. Amer. med. Ass.*, 1960, **174**, 166.

Corticosteroids in Infertility

SIR,—After reading the paper by Drs. D. Ferriman, A. W. Purdie, and W. J. Tindall on the use of corticosteroids in infertility associated with hirsuties and oligomenorrhoea (April 8, p. 1006), I would like to report our experience on that matter.

During the last seven years, we have been trying corticosteroids in the management of ovarian dysfunction sterility, resulting from mild post-pubertal adrenal virilism. In these patients we consider the underlying defect to be a latent, biologically inferior, enzymatic hydroxylation system which is brought to light by stressful stimuli, such as the changing conditions of puberty. The accompanying diagram represents the possible explanation of the ovarian dysfunction and shows how the corticosteroids may act.



Schematic presentation of the altered adreno-pituitary-ovarian interrelation in congenital adrenal hyperplasia.

Nine out of our fifteen carefully selected patients suffering from mild adrenogenitalism and ovarian dysfunction sterility[1] resumed regular menstruation, showed regression of hirsutism, ovulated, conceived, and delivered normal babies. These patients received a 15-weeks course of hydrocortisone, 80–100 mg. daily in divided dosage for the first three weeks, then 60 mg. daily during the next three weeks, 40 mg. for three weeks, and lastly 20 mg. daily in two divided doses for another six weeks. Out of our nine cases, four conceived during the withdrawal period of hydrocortisone therapy, while the remaining five got pregnant within four months of the resumption of the ovulatory cycles. Three out of our nine cases got pregnant for a second time without resorting to any treatment. Only one of the remaining nine got pregnant after a second course of hydrocortisone.

The administered cortisone seemed to be able to restore to normal the disturbed pituitary-adrenal-ovarian relation and to re-establish normal ovarian function.—I am, etc.,

M. H. GHANEM.

Metabolic, Hypertension, and Arthritis Research Center,
Alexandria University, Egypt, U.A.R.

Ice-packs after Episiotomy

SIR,—I do not doubt that cold packs may alleviate the discomfort of a painful perineum, but I am disturbed by the implication contained in the letter by Professor J. H. M. Pinkerton and Dr. R. W. Beard (May 27, p. 1536) that an episiotomy, or even a simple perineal laceration, is commonly followed by pain. I believe that it is not. I cannot give percentages to put alongside the 40% "painful" or "very painful" tabled in their letter, but I should have to think back many years to recall such events in my own practice.

Common causes of pain are, I believe, too tight suturing, inaccurate suturing, or the use of through-and-through skin sutures. Trouble may also arise if the perineum is burdened with too much suture material; an inexperienced house-officer determined to make a good job of things sometimes overloads the tissue with thick catgut, and—what is perhaps even more important—with numerous catgut knots, some of them just below the skin edge. Pain may also be an indication of wound sepsis, but this in itself is often the result of a poor technique, for an accurately sutured episiotomy almost always heals with remarkable completeness and rapidity.

For many years I have used, whenever practicable, midline perineotomy in preference to episiotomy, and have sutured the wound with a simple over-and-over stitch of very fine catgut (*B.P.C.* medium chromic, No. 2/0 size). A long strand mounted on a Mayo trochar-pointed needle (half-circle, No. 3 size) is first inserted at the level of the carunculae myrtiformes and is used as a submucosal stitch to unite the vaginal wall. Continuing with the same strand, the deeper structures of the perineum are brought together—two or three turns are usually sufficient—and the remainder of the perineum then approximated almost to skin level. A subcuticular stitch (still using the same strand of catgut) finishes off the repair, and, if carefully employed, brings about perfect skin apposition. (This stitch must not, however, *penetrate* the skin, for post-operative pain would then be caused.) The long end of the suture is tied to the starting end, which has been intentionally left uncut. Thus, only one knot is used in the whole of the repair, and this is situated below the level of the sensitive perineal skin. This type of repair completely restores normal anatomy and leaves a skin wound that is barely visible.

As I have long been interested in the technique of the operation, I have invariably made a careful inspection and palpation at the post-natal examination and have always questioned the patient on the subject of pain. Many declare that they have had none at all, and some seem to have forgotten that they even had a perineal repair. Others admit to having had a trifling discomfort, but only for the first 24 or 48 hours.

While it is not the main theme of this letter, I cannot refrain from adding how distressed I am to find that many practitioners, even to-day, pay little attention to the finesse of perineal repair—a fact all too obvious at

any gynaecological clinic. I often sadly reflect that comparable stitching—or lack of stitching—on a visible part of the patient's anatomy might be followed by some very awkward questions.—I am, etc.,

Nuffield Department of Obstetrics and Gynaecology, University of Oxford. J. CHASSAR MOIR.

Maternity Units

SIR,—I was surprised and disconcerted to see in your columns (May 27, p. 1543) an attack on Professor Norman Morris, provoked by a lecture he delivered at the Royal Society of Health Conference at Blackpool. He had been invited to address an audience of health workers and architects on the design and requirements of a modern maternity hospital.

I have before me the script of the lecture, and can find no basis for the allegation that Professor Morris attempted "to convey the impression that his was a lone voice crying in the wilderness and that all other obstetricians were blind to the requirements of their profession." Nor do I see any evidence for the suggestion that Professor Morris's paper is liable to raise undue alarm in expectant mothers. Many of our hospital buildings are out of date, and expectant mothers know this only too well. They also know there is a great shortage of beds and they are fortunate to get into any unit, even in a building two hundred years old.

However, the phrases "dreary halls," "human cattle markets," "windy corridors," "conveyer-belts," etc., taken out of context, as they were, by reporters hoping to cause a sensation, give a totally misleading impression of the tenor of the lecture and the discussion that followed. I cannot imagine that Mr. Marshall Scott and Dr. Law are the sort of men who would choose to attack the reformer rather than face the problems of reform, so I can only conclude they did not attend the conference but relied for their information on superficial newspaper reports.—I am, etc.,

London N.W.3. J. M. SLATTERY.

Prevention of Rh Haemolytic Disease

SIR,—I should like to refer to the paper by Dr. R. Finn and his colleagues (May 27, p. 1486) and your leading article (p. 1519) on the prevention of Rh haemolytic disease.

"If foetal Rh sensitization is due to foetal red cells entering the maternal circulation, it seems possible that they may be eliminated before they have time to act as Rh antigens—for example, foetal cells containing A antigen would be removed by a maternal serum containing anti-A."[1] There appear to be two inconsistencies here: (i) "Elimination" means haemolysis, and the products of "elimination" will be absorbed by the cells of the maternal reticulo-endothelial system and will not just "go up in smoke." (ii) Whole red cells from the foetus—or the products of haemolysis of those cells ("elimination")—by nature of their incompatibility will stimulate antibody formation in the cells of the reticulo-endothelial system of the mother.

There is no doubt that the red cells of the foetus do enter the circulation of the mother as a result of leakage through the very thin-walled capillaries of the placenta. There is no doubt that this leakage is more frequent than generally realized. If the red cells of the foetus remain in the maternal circulation for a prolonged period, it is likely that nothing will happen so long as the foetal cells *do* remain in the mother's circulation; it is probable that only after "elimination" do antibodies begin to be formed. Anti-Rh-bodies are of two kinds: (*a*) "saline" agglutinins, and (*b*) "albumin" agglutinins. The "saline" antibody has a large molecule (sedimentation coefficient 19 S approximately), and the "albumin" antibody has a small molecule (sedimentation coefficient 7 S approximately).[2] Injection of the Rhesus-negative pregnant mother with "saline" agglutinins probably would not harm the foetus. A very different state of affairs would follow the injection of "albumin" agglutinins into the pregnant mother.

Why not treat the mother with steroids and prevent the cells of her reticulo-endothelial system from reacting to the foreign proteins?[3]—I am, etc.,

Pathology Department, St. Margaret's Hospital, Epping, Essex. FRANK MARSH.

REFERENCES

1 Race, R. R., and Sanger, R., *Blood Groups in Man*, 1958, 3rd ed., p. 315. Blackwell, Oxford.
2 Campbell, D. H., Sturgeon, P., and Vinograd, J. R., *Science*, 1955, **122**, 1091.
3 Marsh, F., *Lancet*, 1961, **1**, 455.

Cervical Carcinoma in a Girl

SIR,—I was greatly interested in the case report by Mr. C. J. B. Orr and Mr. P. R. B. Pedlow (May 27, p. 1511), having had under my care recently a young, single girl presenting some similar features.

When she was first seen in the out-patients' clinic, immediate admission to hospital was imperative because of bleeding. This increased during the next few days, and several pints of blood were transfused. Whilst transfer was being arranged to the radiotherapy centre, some considerable distance from her home, it was emphasized that the bleeding, which was copious despite continued tranfusion, would not be stopped immediately by the initial cancericidal dose. With the full concurrence of my colleague in radiotherapy, it thus became clear that hysterectomy was an urgent necessity to effect haemostasis, quite apart from the merits of surgical treatment as opposed to radiotherapy. I therefore carried out a radical procedure on the evening of Easter Saturday. She made a very rapid and entirely uneventful recovery, and has now returned to work full of youth and vigour. The ultimate outlook is obviously another matter.

I was, of course, aware of the paper by McCall *et al.*,[1] in which they recommended conservation of functioning ovarian tissue in the very young, but I decided, rightly or wrongly, not to conserve either appendage. The excised uterus presented an almost identical picture to that shown in Fig. 2 of their article. My patient appears so far to have no ill effects whatever from total extirpation of ovarian tissue, and in general one feels that surgical treatment is to be preferred in the very young woman, and, though in this instance radiotherapy was at first chosen, surgery was, of course, forced upon us subsequently.

I was also most interested to learn that the search of the literature had revealed no case below the age of 18; my patient was aged 17, and might therefore be the youngest case yet recorded.—I am, etc.,

Liverpool 1. H. V. CORBETT.

REFERENCE

1 McCall, M. L., Keaty, E. C., and Thompson, J. D., *Amer. J. Obstet. Gynec.*, 1958, **75**, 590.

Safety Belts in Cars

SIR,—The Minister of Health has just reminded us in his Winchester Address (May 27, p. 1479), that his duty under the National Health Service Act, 1946, includes "to promote the establishment of a comprehensive health service designed to secure . . . the prevention . . . of illness" and "to provide, or secure the effective provision of, services." He has interpreted "illness" in the past to include injuries, as, for example, in the home.

For some months past the fitting of cars with safety belts has been progressing rapidly. Some private companies and some taxi services are already equipped. Four cases have come under my observation in the last year. Two patients were involved in accidents in cars not fitted with safety belts. Both received broken noses and other injuries, necessitating weeks in hospital and several weeks from work. One still suffers from loss of the sense of smell, the other from a lack of confidence in cars, a serious handicap in his work. The other two were involved in accidents while wearing safety belts. One ran into the back of a lorry so hard that the car was completely written off as beyond repair. The other turned his car upside-down and travelled in it 150 yards (135 metres) on the roof. Neither of these two received any injury or permanent upset as a result of the accident.

Four cases are not statistical evidence, not even added to Mr. Donald Campbell's miraculous escape, but much statistical evidence must now be available to confirm that safety belts save lives, reduce the number and severity of injuries, and probably the number of road accidents. The driver wearing a belt is less likely to be thrown out of his seat by sudden swerves and more likely to retain control of his car.

Although some car manufacturers have announced that some new models will be fitted with safety belts and one American insurance company has announced a reduction in the premium for cars with belts, much more initiative is needed to encourage this injury-reducing measure. The Minister of Health might well have statistics collected to persuade insurance companies that it is good business to encourage the provision of safety belts by reducing premiums on cars so fitted. He might also persuade his fellow Minister that road casualties can be so reduced, and suggest the reduction of road-fund licences on cars so fitted. There is seldom such a clear case for such a simple measure to reduce deaths and human suffering.—I am, etc.,

Gerrards Cross, Bucks. ROBERT PIPER.

SIR,—Dr. A. Ward Gardner in his letter (May 20, p. 1463) refers to a possible association between whiplash injury of the neck and shoulder straps. I have not heard of this association; in the two cases I know of personally and others I have read about the injury was due to the patient's car being run into from behind. A head-high seat back would have prevented this injury, but safety belts would have had no effect one way or the other.

I am sure that the best belt is the combination of lap-strap and diagonal belt referred to in Dr. Gardner's letter, but if a simpler belt is wanted the diagonal belt appears preferable to the lap-strap, as it prevents facial injury and concussion although not lower-limb injury.—I am, etc.,

Public Health Department, Purley, Surrey. J. B. MORWOOD.

SIR,—As one who is pursuing, in a small way, investigations into the mechanism of injury in car occupants, I was interested to see Dr. A. Ward Gardner's letter on safety belts (May 20, p. 1463). With due respect, Colonel Stapp's experiments do not necessarily reflect the pattern of injury in road accidents in this country. The danger of whiplash injury—unpleasant though it is—seems hardly as great as that of facial injury—for example, fractured jaws—which are much commoner.

Incidentally, I have just had a combined harness fitted to my car.—I am, etc.,

Leeds 10. PETER WINTERSGILL.

Pernicious Anaemia in Jamaica

SIR,—I am very glad to see that in response to Dr. S. J. Baker (April 8, p. 1038) Dr. Richard Asher (May 6, p. 1316) has drawn attention again to the very frequent occurrence of anorexia, loss of weight, and various gastro-intestinal symptoms in pernicious anaemia. So many recent authors do not apparently read or else ignore the older literature on this subject and tend to make or accept broad statements and opinions without referring to original and factual publications. It is a very long time ago since I drew attention to these particular features, but reference to the *British Encyclopaedia of Medicine*, vol. 1 in the 1936 edition (and also to others of my publications prior to and since that date), will show the following under "Clinical Picture in Pernicious Anaemia":

"... These are mainly dyspepsia (80 per cent), flatulence (70 per cent), fullness after taking food (46 per cent), nausea, vomiting (56 per cent) or constipation (46 per cent), diarrhoea (25 per cent) and soreness of the tongue (61 per cent), sometimes even going on to ulceration. Epigastric pain and abdominal tenderness or soreness are common. Dysphagia and koilonychia are extremely rare (cf. hypochromic anaemia). Contrary to the general view there is often well-marked loss of weight and the condition may simulate gastric carcinoma."

These observations, all of which are contrary to Dr. S. J. Baker's statement, were based on observations made on several hundred patients and more recently on more than 3,000 of my patients with pernicious anaemia. I make no apology for reinforcing Dr. Asher's comments, because so many in recent years have made new "discoveries" about the clinical and other features of pernicious anaemia which have all been quite well known for more than 30 years, as these modern authors would find if they would read the earlier publications.—I am, etc.,

Department of Haematology, The Royal Infirmary, Manchester 13. JOHN F. WILKINSON.

Secondment Abroad

SIR,—Mr. D. R. Richard's article on his experiences in Northern Nigeria (May 13, p. 1382) is not only intrinsically interesting but also has a historic significance which deserves appreciation. At a period in our professional history when successive Presidents of the British Medical Association have chosen as the subject for their presidential addresses "Commonwealth and Common Health" (June 25, 1960, p. 1907) and "Medicine and Health on a Commonwealth Basis" (February 11, 1961, p. 375) it is heartening to read this example of a successful secondment from the National

Health Service. It is of interest to note that Mr. Richard, seconded to Nigeria as a registrar, is able about a year after his return to this country to write from a senior registrar post in the Royal National Orthopaedic Hospital, London.

Much difficulty has been experienced in finding ways and means by which our doctors can help in the under-doctored countries and return to our National Health Service without "losing the place." Universities have sponsored proleptic appointments from teaching hospitals and these have usually been to university centres. This is the first description I have read describing a secondment of this kind: from a hospital in this country to a non-teaching hospital in a country such as Nigeria. One would like to think that this kind of experience could be multiplied. The idea of establishing a regular relationship of this kind between hospitals in this country and hospitals abroad seems excellent.

One would like to know at what stage in his registrarship Mr. Richard went to Nigeria. Did he have his senior registrarship "all tied up" before he went, or did he have to apply for it from abroad, and how did his advisory appointments committee evaluate his experience in Nigeria in a non-teaching hospital? This kind of appointment needs further study. At what stage is it of most value to the doctor and to the country he visits—registrar, senior registrar, consultant, perhaps even house officer? What length of stay is most valuable to both?

The wealth of clinical material is undeniable. The kind of case described in Mr. Richard's article could be matched in many other countries. In my own experience in South Arabia[1] the cases of osteomyelitis and leg ulcers could be exactly paralleled. Similar ulcer cases were described by Buchanan and Sanderson in Somaliland[2] and I have also seen them in Jamaica. After several years of "amputating legs and supplying pegs" as described in Mr. Richard's article, it was pointed out to me that something might be done to prevent these ulcers developing to the stage where amputation is necessary. The villages from which the worst ulcers came were visited. Village dressers were recruited and trained to treat simple wounds and teach cleanliness. The incidence of severe leg ulcer from these areas fell markedly and rapidly. The need for surgeons to treat individual sufferers is great. The wealth of experience open to public health doctors in these situations is equally valuable and the opportunity for preventive medicine is tremendous.

Planned secondment of doctors in various stages in their careers and from various branches of our profession is overdue. In his presidential address already referred to Sir Douglas Robb did not confine his vision to the Commonwealth, though that would seem a useful field in which to begin. A properly planned scheme of this kind could bring valuable experience to many of our doctors—experience of a kind not otherwise available; would bring benefits to thousands of suffering individuals; and could do great good to international relationships and the general increase of good will in the world.—I am, etc.,

Edinburgh 9. P. W. R. PETRIE.

REFERENCES

[1] Petrie, P. W. R., *A Medical Survey of the Western Aden Protectorate*, 1943. Colonial Office, Middle East, Pamphlet No. 66. H.M.S.O., London.
[2] Buchanan, J. C. R., and Sanderson, I., *Trans. roy. Soc. trop. Med. Hyg.*, 1935, **28**, 505.

Scorpion Stings

SIR,—Scorpion stings are especially fatal in the Cuddapah District of Andhra Pradesh, Madras, India. When I was attached to the Government Headquarters Hospital, Cuddapah, from 1946 to 1948, I was surprised to see robust youths dying after scorpion stings in spite of all available treatment. Sweating, bradycardia, and exhaustion were prominent besides the pain at the site of the sting. The poison appears to act as a direct cardiac poison. It is the fair slim scorpion which is more deadly than the big black or dark one, because the latter is sluggish, probably owing to its weight, and it takes a longer time to sting.

Dr. P. M. Mundle (April 8, p. 1042) says "specific antiserum is not available." Well, it has been available for over decades in the King Institute, Guindy, Madras, as "antiscorpion serum," and many hospitals get their supplies from this institute. I found the serum of value especially in children, and perhaps useful in cases where a high lethal dose had not been injected by the sting. But in my own personal experience I found the best treatment was to scarify the site of the sting and squeeze out the poison very soon after the smarting sting. The result was dramatic; throbbing pain vanished, leaving only a slight burn which in turn disappeared in an hour or two.—I am, etc.,

Madras, India. V. N. VISVANATHAN.

Acute Diabetic Abdomen

SIR,—I should have thought that the "acute diabetic abdomen" in the *known* diabetic was too well known to merit space in your correspondence columns. "In infancy and childhood diabetes mellitus may progress very rapidly and the patient may first present in the stage of pre-coma with a history of constipation and anorexia and upper abdominal pain. . . ." This has been standard undergraduate teaching in the course of paediatric surgery in the Glasgow Medical School for more than a quarter of a century. I suggest that Dr. K. Lancer's (April 29, p. 1246) teachers and his reading material are more typical of British medicine than Dr. P. Edward Dipple (May 27, p. 1539) realizes.

In a large children's hospital, the "acute diabetic abdomen," although well known, is rare. But it is not uncommon for children to be admitted to hospital in a dehydrated condition with abdominal pain, vomiting, and ketosis; a specimen of urine may not be immediately available. It is common practice to rehydrate such patients with intravenous glucose-saline. A specimen of urine obtained after the child is hydrated may show gross glycosuria and the blood-sugar may be over 300 mg./100 ml. in a non-diabetic child. If this information was available in the more common textbooks of medicine there might be less delay in surgical intervention in the child suffering from an acute abdominal catastrophe.—I am, etc.,

Royal Hospital for Sick Children, Glasgow C.3. W. M. DENNISON.

REFERENCE

[1] White, M., and Dennison, W. M., *Surgery in Infancy and Childhood*, 1958, p. 163. Livingstone, Edinburgh and London.

SIR,—I hope that the result of this interesting correspondence will not be the neglect of the possibility of an acute abdominal emergency occurring with diabetic ketosis. Ketosis is usually precipitated by one of the following: "(1) infections of the respiratory,

genito-urinary, or gastro-intestinal tract, or pyogenic infections; (2) surgical procedures or trauma; (3) gastro-intestinal disturbances with reduction of food intake or vomiting."[1] Therefore acute abdomen with several of these factors operating may precipitate diabetic ketosis.

Diabetes itself could also be a contributory factor in an acute abdominal condition—namely, mesenteric occlusion. Atherosclerosis, which is common in diabetics, and the fluid loss due to vomiting and polyuria would predispose to this condition. I have seen such a case which was sent to casualty as an acute abdomen, was diagnosed there on routine urine testing as a diabetic precoma, and ultimately died with gangrene affecting the whole of the small bowel. Indeed, I wonder if some cases of "diabetic acute abdomen" may not be due to mesenteric insufficiency, in other words "abdominal angina" not going on to a major thrombosis.—I am, etc.,

London N.W.3. I. T. LORENTZ.

REFERENCE

[1] Cecil, R. L., and Loeb, R. F., *A Textbook of Medicine*, 1959, 10th ed., p. 621. Saunders, Philadelphia.

SIR,—The correspondence on the acute abdomen prompts me to mention yet another cause of abdominal pain which can lead to confusion. On at least two occasions I have had dealings with patients referred as "? appendicitis" who were in fact suffering from an early stage of poliomyelitis. On questioning, however, both stated that their headache was more severe than their abdominal pain. Abdominal examinations failed to reveal any definite signs, but both had stiff necks and both later developed some paralysis. An operation would not have improved their chances of complete recovery.

Dr. A. K. Chatterjee (May 27, p. 1539) gives a by no means complete list of medical causes of abdominal pain. In his excellent book *The Early Diagnosis of the Acute Abdomen* Sir Zachary Cope[1] mentions influenza, typhoid, tuberculous peritonitis, epidemic pleurodynia, the congested liver of cardiac failure, and leukaemia. No doubt our medical colleagues could enlighten us still further.

I am not quite sure what Dr. Chatterjee means by saying that "the diagnosis of acute abdomen is no longer within the province of the surgeon." Is not the word "entirely" missing from the phrase? There is no doubt, however, that a timely medical consultation is sometimes most helpful.—I am, etc.,

Dunn Laboratories, St. Bartholomew's Hospital, London E.C.1. A. P. WYATT.

REFERENCE

[1] Cope, V. Z., *The Early Diagnosis of the Acute Abdomen*, 11th edition, 1957. Oxford University Press, London.

Intravenous Laevulose in Malignant Disease

SIR,—During the past two years intravenous laevulose has been used at this centre for supportive therapy. The preparation employed has been "laevosan," given as an intravenous injection in the amounts suggested by the makers.

There was a group of patients who experienced anorexia associated with nausea during courses of deep *x*-ray therapy on fairly extensive fields. Such cases were given 40% laevulose, 20–40 ml. daily. This alleviated nausea and, in addition, produced a feeling of well-being. In cases experiencing dysphagia associated with pharyngeal, laryngeal, and oesophageal tumours, laevulose was used in larger doses—40–60 ml. of the 40% solution being given daily, first during the early stages of treatment and again during the later stages and the period of reaction to radiation, when swallowing was difficult. In cases where there was a degree of bowel obstruction—such as occurs in cases of reticulo-endothelial neoplasm—with consequent vomiting of food, laevulose not only improved the patients' general condition but the amount of vomiting also lessened. Similarly hiccup, as a symptom of bowel obstruction, was noticeably relieved. In addition to this, the patients were comforted and tended to rest and sleep during the period following the injection.

Terminal cases who were cachectic also benefited from intravenous laevulose, which mitigated their distress associated with semi-starvation. Elderly patients, upon whom deep *x*-ray therapy imposes considerable strain, were also given laevulose with good effect.

It has not, so far, been possible to obtain a sufficiently large series of biochemical investigations on cases to whom laevulose has been given to enable workers at this centre to assess its physiological effects. On a clinical assessment it would appear that intravenous laevulose provides a very valuable source of supportive therapy, greatly beneficial to the above classes of patients, none of whom showed any evidence of undesirable side-effects. In most cases the use of glucose would, in fact, not have been practicable owing to the disadvantages associated with the administration of intravenous solutions of glucose over periods of more than a few days. Laevulose appears to have minimal deleterious effects on the veins, it being possible to use the same vein repeatedly. In addition, it appeared that the patients' improved general condition caused them to attempt to take nourishment by mouth to a greater extent than they would otherwise have done, which obviated the necessity for combating dehydration with prolonged administration of intravenous fluids. This was considered to be an extremely satisfactory aspect of laevulose therapy.—I am, etc.,

MARGERY WILLIAMS.

Northern Ireland Radiotherapy Centre, Belfast.

"Persantin"

SIR,—I have been interested in the correspondence concerning the recently introduced coronary vasodilator drug "persantin." As Dr. F. J. A. Bateman (April 15, p. 1108) states, there appears to be no doubt that it is an effective dilator of the coronary vessels, at least in the healthy dog.

Following development of a technique of coronary arteriography[1] in our laboratory, we thought it might be interesting to observe the effect of alleged coronary vasodilators on coronary arteriograms. Following intravenous persantin in dosage of 0.3 mg. per kg. in dogs, coronary arteriograms show definite dilatation of the main coronary vessels, the diameters increasing by 25 to 30%. In addition much more detailed arteriograms are obtained due to better filling of the smaller vessels. These effects come on within two minutes of injection and last for 30 to 45 minutes. While we have been unable to measure total coronary blood-flow satisfactorily (has anyone?) we have observed a change in coronary sinus blood-oxygen saturation from 31 to 70% following a similar dose of persantin intravenously. Furthermore, direct recording of pressure in the

coronary arteries shows a synchronous widening of the coronary pulse-pressure, and coronary circulation-time is reduced by approximately 30%. An interpretation of these observations is that the coronary flow is considerably increased by this drug in healthy dogs.

Glycerin trinitrate will also dilate the proximal coronary vessels. For some reason, possibly reduced flow, the distal vessels are difficult to demonstrate arteriographically when this drug has been given. Little or no change occurs in the coronary sinus blood-oxygen saturation following administration of glycerin trinitrate.

These are recent observations which need further study. I am told that other workers besides Dr. D. C. Deuchar (April 1, p. 967) have noted that persantin does not necessarily relieve angina pectoris, though in subjects to whom the drug is administered coronary sinus blood-oxygen saturation rises. The same subjects obtained relief of pain from glycerin trinitrate.[2] I am unable to state whether persantin was given by the oral or intravenous route in these studies. Could it be that, in the diseased coronary tree, vasodilators are unable to improve blood flow through ischaemic areas and release of pain-producing metabolites proceeds as usual? Glycerin trinitrate may exert its pain-relieving effect by a totally different mechanism—for instance, by interfering with myocardial metabolism and reducing the production of pain-producing metabolites. We have observed a considerable fall in aortic pressure following administration of glycerin trinitrate to dogs. Cardiac-output studies need to be done under these circumstances. Another possibility to be considered is that persantin may open arteriovenous anastomoses in the coronary circulation. This would account for some of the observed effects.

My own theoretical objection to the use of vasodilators in the treatment of arterial occlusive disease affecting muscle is that it is unreasonable to expect pharmacological vasodilators to do what the extremely potent tissue-metabolites cannot. What will be of interest will be to see if persantin can promote the development of coronary anastomotic channels. I understand that work on these lines is proceeding.[2]—I am, etc.,

University Hospital, University of Saskatchewan, Saskatoon, Sask., Canada. NEVILLE J. JACKSON.

REFERENCES

[1] Jackson, N. J., and Cobbold, R., *Canad. med. Ass. J.*, 1961 (in press).
[2] Efford, R. J., personal communication.

SIR,—During the past three months I have treated 15 cases of severe myocardial disease with "persantin." They included both men and women and their ages ranged from 50 to 75 years (six were over 70). All showed myocardial insufficiency presumably due to coronary atherosclerosis. The major symptom was dyspnoea resulting in severe limitation of exercise tolerance; all were ambulant. From time to time their ankles swelled and there was transient hepatomegaly; all except one were fibrillating. There were no cases of valvular disease and the blood-pressure in all was normal for their age. This type of case is common in general practice and their disability often remains constant for months or years. All the cases in the present series were receiving digoxin in adequate maintenance doses and no other regular treatment was being given.

Seven cases started treatment with intravenous persantin, 10 mg. daily for 14 days, before going on to oral treatment, 50 mg. t.d.s. The remainder were given the drug orally from the start. All except one showed an improvement in dyspnoea, and declared their exercise tolerance (ability to walk up hills, stairs, etc.) to be much greater. They expressed a sense of well-being that they had not enjoyed for a long time. Two cases ceased fibrillating and in one case the urine became albumin-free for the first time in years. In two cases receiving intravenous therapy there was a marked diuresis on the first day.

The effectiveness of vasodilating drugs in coronary artery disease must depend on the ability of the vessels to dilate, and this in turn depends on the ratio of the remaining plain muscle to fibrous sclerotic replacement. The greater the latter, the more rigid the arterial wall and the less effective any vasodilator. This, I feel, must explain the varying experience of your correspondents with persantin. The shortest period of observation in any of my cases is six weeks and the longest three and a half months; to date there have been no relapses.—I am, etc.,

Stourton, Near Stourbridge, Worcs. J. P. ADLAM.

Sexual Offences Against Children

SIR,—There appears to be a noticeable increase of late in sexual offences against children, those resulting in the death of the child being reported in banner headlines in the press. This particular perversion has also received the attention at the hands of novelists, and although it may be that publicity has, to some extent, had the effect of warning parents against this danger to their children, I cannot but feel that it has given rise to a stimulus, particularly in the case of subnormal types and those with perverted sexual tendencies, that has the effect of increasing these crimes.

That there is great public interest in the details of such cases there can be doubt, but there are countries where such news is considered of less importance which must receive the impression that sexual perversions are far more prevalent over here than is actually the case. It would be interesting to hear the views of psychiatrists on the effect of this publicity.—I am, etc.,

London S.W.7. J. N. LORING.

Advertising and Teenage Behaviour

SIR,—Dr. Clifford Allen (May 13, p. 1392) has directed attention to a social problem of the utmost concern at the present time—namely, the recent increase in offences of drunkenness in teenagers. Dr. Allen believes this to be directly due to advertising trends which are now being intensively directed towards young people since they are regarded as constituting a significant potential source of increased sales. In his view "the responsibility falls directly on the advertisers whose subtle propaganda is deliberately concerned with persuading teenagers to start drinking." Much the same might be said of the similar though socially less disastrous practice of excessive smoking by adolescents, who are also now being subjected to intensive propaganda by cigarette manufacturers who are now said to be "concentrating their promotional efforts on teenagers and other young smokers who are not yet set in their ways."[1]

The excessive smoker mainly harms himself. The damage that the excessive drinker inflicts is by no means so restricted: the social and economic

consequences of alcoholism are widespread and its prevention must be a matter of concern to all. Propaganda must be met by a true presentation of the facts by every available means, including greatly increased health instruction in schools. Unfortunately the present trend is in a precisely contrary direction, for as Professor J. D. Hay[2] has emphasized the lack of attention which the problem of alcoholism receives from the Government would seem to apply especially to the Board of Education. In the 1940 edition of the Board's handbook, *Health Education*, a handbook of suggestions for teachers and others concerned in the health education of young people, there was, for example, a satisfactory chapter on alcoholism. In the 1956 edition of the booklet this was reduced to a little over one page. Professor Hay concludes, "As the soundest basis for achieving a reduction in alcoholism in this country is education of the population, and especially of the children, the Board of Education would seem to have taken a most unwise and short-sighted step in reducing in this way the information concerning alcohol available to teachers and, through them, to our children." Many will wonder what is actually being *done* in this vitally important matter. For surely we cannot continue to drift indefinitely towards progressive social deterioration as the teenage drinker of to-day becomes the confirmed alcoholic of to-morrow.—I am, etc.,

Carter Foundation, London W.1. BASIL MERRIMAN.

REFERENCES

[1] Lipetz, S., *Lancet*, 1960, **2**, 978.
[2] Hay, J. D., ibid., 1960, **2**, 813.

SIR,—The letter from Dr. Clifford Allen (May 13, p. 1392) draws our attention to an increasing problem of teenage drunkenness in Britain. Two months ago our attention was focused on a recrudescence of venereal disease (April 29, p. 1247). Perhaps the two problems are related.

Teenagers are very open to suggestion. Many of us can remember the turbulent times of adolescence and may well have reason to murmur, "There, but for the grace of God, go I." Surely it is the responsibility of the older generations to protect the younger.

May I therefore, as a resident of Israel and only an occasional visitor to Britain, say how much I deplore the intensive advertising mentioned by Dr. Allen, and also the heavy advertising for contraceptives. It is quite difficult to find a hairdresser who does not display an advertisement for one or more brands of contraceptive. If the people of Britain think that promiscuous behaviour is undesirable it would be worth investigating what proportion of contraceptive devices are being sold to the unmarried youths of Britain and whether the extensive and intensive advertising should not be curbed.—I am, etc.,

Nazareth, Israel. JOHN L. TESTER.

SIR,—Dr. Clifford Allen's timely remarks on the advertising of alcoholic drinks (May 13, p. 1392) apply with double force to cigarettes. Constantly reminded of its supposed status-value, many young people are only dimly aware of the unpleasant, dangerous, and even fatal sequelae of smoking. One way for the medical profession to inform them is to meet the tobacco moguls on their own ground. If a sum of money were available for this purpose, I can think of no better way of using it than to make a short film, for general showing between the advertisements, hinting at some of the end-results of this addiction. The stars could be found in any hospital ward in winter.

Anybody sufficiently frightened to go to his G.P. could then be told the facts so far as they are at present known.—I am, etc.,

London S.W.3. JOHN PLAYFAIR.

Feeding of Infants before Adoption

SIR,—Owing to the rising incidence of unmarried mothers and the unwanted child, might I ask for space in your columns to air this very difficult problem? General debate would perhaps help to enlighten this much-discussed and increasingly difficult situation. The present opposing points of view leave much to be desired.

One school of thought, encouraged by many grandmothers, condones the unmarried mothers' attitude, and holds that the mother should not see, or be in any way responsible for, her baby if the child is to be adopted. The resulting problem of feeding in this case is obvious. The opposing view stresses that the mothers should be helped to realize that they have a definite responsibility towards the child as an important life in relation to the mother and to the community generally.

At times 25% of patients in a maternity unit may be unmarried. There is here a moral-welfare and psychological problem for the future well-being of the unmarried mother, who with help and understanding may wish to nurse her baby, and with encouragement would probably develop a natural maternal interest in the future of the child.

There appears to be a discrepancy of opinion in this matter of care and feeding between doctors on one hand and the secretaries of the adoption societies on the other.—I am, etc.,

Windsor, Berks. D. MAXWELL.

"Virugon" in the Treatment of Warts

SIR,—Dr. O. A. Finn's unsuccessful experience in treating warts with "virugon" (March 25, p. 904) is similar to my own. Separate double-blind controlled trials were carried out on 40 patients with ordinary warts and 30 patients with plantar warts. The patients were referred to the dispensary and given virugon or identical placebo tablets according to previously prepared random lists. The dosage used was one tablet three times a day for three weeks for patients under 14 years, and two tablets three times a day for those above this age. No local treatment was used. Clinical assessment was made at three weeks and again at six weeks after starting the tablets. At the end of the completed trials the allocation of patients to treated and control groups was revealed and correlation with clinical progress made. Improvement was considered to have occurred if one or more warts had disappeared or if plantar warts had darkened. The results are as follows:

		Ordinary Warts		Plantar Warts	
		Virugon	Placebo	Virugon	Placebo
Number of patients		20	20	15	15
At 3 weeks:	All warts gone	0	1	0	1
	Improved	4	3	2	1
	No change	16	16	13	13
„ 6 „	All warts gone	2	3	1	3
	Improved	2	1	3	2
	No change	16	16	11	10

These results confirm that virugon, in the above dose, does not influence the course of warts. This is disappointing, as present local methods are either unpleasant or ineffective. I feel, therefore, that efforts to find an effective systemic treatment for warts should continue.

In the meanwhile, prophylactic measures to prevent the spread of infection should be encouraged. Much could be done to prevent the spread of plantar warts by regular foot inspections in the schools, by the exclusion of children known to have plantar warts from swimming-baths and showers, and by discouraging the present trend towards doing physical training in bare feet. I am sure that 30 minutes' exercise without shoes each week is only a sop to educationists' theory and has no practical value in helping the normal development of feet. In my experience, mothers are only too willing to provide plimsolls for their children.

I am grateful to Dr. F. F. Hellier and Dr. S. T. Anning for allowing me to treat their patients. Bayer Products supplied the virugon and placebo tablets used in these trials.

—I am, etc.,

Skin Department, The General Infirmary, Leeds 1. NEVILLE ROWELL.

E.C.H.O. Type 9 Outbreak

SIR,—May I correct a misunderstanding on the part of Drs. F. L. Constable and L. F. Howitt, whose article on an outbreak of E.C.H.O. type 9 infection in a children's home appeared in the issue of the *Journal* of May 27 (p. 1483)? The report which they cite (Landsman *et al.*, 1960) appeared in the month of August and began, "During the past month we have encountered in practice an outbreak of febrile illness in children, of which the presenting features were rash, adenitis, headache, and vomiting." These cases were occurring in Glasgow at the same time as those reported by the authors from Edinburgh, and not, as suggested by them, in 1959. A detailed report of the Glasgow outbreak is in course of preparation.—I am, etc.,

Department of Infectious Diseases, Brownlee Laboratory, Ruchill Hospital, Glasgow N.W. JOAN B. LANDSMAN.

Unintelligible Initials

SIR,—During the late war we were familiar with initials conveying to the initiated various endearing (or other) messages. Their number and complexity increased as the period of hostilities lengthened. At last the authorities put a limit to their use, as they could be made to convey secret information which infringed security.

It is about time that editorial feet stamped firmly on the vast growing number of initials used in medical articles, which initials convey little if any meaning to a large proportion of your readers.

In your issue of May 27 I see an article entitled: "Outbreak of E.C.H.O. Type 9 Infection in a Children's Home" (p. 1483). What these initials represent I have not the faintest idea, nor, I suspect, have the great majority of your readers. Is the *Journal* so hard up for space that it cannot afford to add (in brackets) *in extenso* what these stand for? *The Times* crossword is jolly good fun and contains some very abstruse and esoteric clues, but they pale into insignificance before some of your contributors' efforts. Who will understand what they mean in fifty to a hundred years' time? A scientific communication that is not lucid is valueless and is cast on one side by the reader. Lucidity is the hall-mark of the intelligent writer.—I am, etc.,

ST. GEORGE B. DELISLE GRAY.
Woodford Green, Essex.

*** E.C.H.O. viruses are "enteric cytopathogenic human orphan" viruses. The name "orphan" was coined,[1] in a moment of inspiration, by Dr. F. Duran-Reynals, of the Yale University School of Medicine, as appropriate for viruses in search of a disease. Their full title derives from a recommendation of a committee appointed by the Conference on Orphan Viruses held by the National Foundation for Infantile Paralysis in May, 1955, in New York. The E.C.H.O. viruses share the following properties (among others)[2]: (1) They are cytopathogenic for monkey and human tissue-culture cells. (2) They are not neutralized by poliomyelitis and Coxsackie antisera. (3) They are unrelated to other viruses present in throat or intestine and recoverable by inoculation of primate tissue cultures—for example, herpes simplex, influenza, mumps, measles, varicella, and adenovirus. (4) They are neutralized by human gamma globulin, and produce a complement fixing antigen. Nearly 30 antigenically distinct types of E.C.H.O. virus have now been identified.—ED., *B.M.J.*

REFERENCES

[1] Committee on the E.C.H.O. Viruses, *Science*, 1955, **122**, 1187.
[2] Rhodes, A. J., and Rooyen, C. E. van, *Textbook of Virology*, 3rd edition, 1958, p. 473. Baillière, Tindall and Cox, London.

Diabetics and Prescription Charges

SIR,—Sufferers from several chronic diseases who need constant drug treatment to maintain health or even life (rheumatics, anaemics, etc.) will suffer increased hardship from the doubled prescription charge, but none more than the severe diabetic, with his numerous needs at two shillings each item: (1) insulin (one or two types); (2) insulin syringe (B.S.1619); (3) needles (luer-mount); (4) spirit for sterilization ("industrial" is best); (5) cotton wool ("hospital pack" is cheapest, and satisfactory); (6) tablets for urine testing; (7) sulphonylurea tablets; *composite packs*—(*a*) syringe and 2 luer-mount needles and (*b*) urine analysis set.

The Ministry has mitigated the hardship by announcing that the doctor, at his discretion, may prescribe items 1–7 for a long time—even up to three months—irrespective of the *quantity* ordered (and it is hard to imagine any reason for his not doing so). Some practitioners seem unaware of this permission, and this letter is to publicize this fact.

For the information of diabetics, this letter will be published in the *Diabetic Journal*, and, although its policy is never to intervene between patient and doctor, some patients may bring this letter to their doctor's notice.

The Ministry of Health has confirmed that, in the case of hardship, application may be made to the National Assistance Board for help.—I am, etc.,

R. D. LAWRENCE,
Chairman, Executive Council, British Diabetic Association.
London W.1.

Teats

SIR,—I enjoyed the observations of Dr. Rosemary Graham (May 20, p. 1453) on "Teats." Why was she afraid to disclose the names and makers? *Which?* is able to do so. Please could we have Dr. Graham's

BEST BUY for premature babies
BEST BUY for normal neonates
BEST BUY for four-month-old babies?—I am, etc.,

Abbots Langley, Herts. PETER TOMSON.

Obituary

ARNOLD L. GESELL, M.D., Ph.D., Sc.D.

Dr. Arnold L. Gesell, director emeritus of the Clinic of Child Development at Yale University, and formerly professor of child hygiene at the Yale School of Medicine, died after a long illness at his home in New Haven on May 29, aged 80. His lifelong studies of child development brought him international renown, and through his books he became the guide and counsellor to a host of parents in the U.S.A.

Arnold L. Gesell was born in Alma, Wisconsin, on June 21, 1880. He graduated B.Ph. at the University of Wisconsin in 1933 and Ph.D. at Clark University in 1906. After holding a teaching post at the Los Angeles State Normal School he was appointed assistant professor of education at Yale, where he later graduated in medicine. In 1915 he became professor of child hygiene at Yale, where a few years previously he had founded the clinic of child development. He was also attending paediatrician at the New Haven Hospital. After retirement from his academic posts in 1948 he spent four years as research associate with the Harvard Paediatric Study, and he also accepted the presidency of the American Academy for Cerebral Palsy. A Fellow of the National Academy of Sciences, he was also for some years a member of the National Research Council.

Dr. Gesell's studies of children began at birth, and many of his observations were recorded on film as well as in his books. One of his last works was a study of children between 10 and 15 years of age. This, like two of his other well-known works—*Infant and Child in the Culture of To-day* and *The Child from Five to Ten*—were written in collaboration with Dr. Frances L. Ilg. But his output was prodigious, and his books were said to have sold nearly one million copies in the United States alone.

Dr. Gesell is survived by his widow, who was co-author with him of his first book on primary education, and by a son and a daughter.

We are indebted to Professor R. S. ILLINGWORTH for the following appreciation: Though the normal development of the infant and young child had been studied by others, it was Arnold Gesell who popularized the subject and introduced it to the multitudes. He began his studies of normal children some 50 years ago, and since then he has published 35 or more books and innumerable papers, so that he has become known throughout the world. His name is well known in Britain, and I doubt if there are any educated parents in the United States who have not heard of Arnold Gesell. He and his staff put the study of the development of the normal child on to a scientific and statistical basis, and then applied the work to the selection of children for adoption, to the study of the handicapped child, and to developmental prediction in all its aspects.

Workers came to his department from all over the world in order to study his methods, and in his latter years of failing health he must have derived much satisfaction from the knowledge that so many of the leading developmental psychologists in the United States and elsewhere have worked under him, and that his work is continuing in innumerable corners of the earth.

Gesell's method was the very antithesis of that of so many psychologists to-day, who in their efforts to be thoroughly scientific rely entirely on an objective examination for the assessment of a child's potential. No child was studied in Gesell's clinic before a social worker had visited the home, gleaned all relevant information about the environment at home, and determined the infant's normal play period. The time of examination was arranged accordingly, whether morning, afternoon, or evening. A full physical and developmental history was taken by the examiner. The baby was then examined in a room by Gesell or a member of his team, whose running commentary was recorded. The examination was watched by a group of workers through a one-way viewing screen. When the examination was completed, the whole team met and discussed the assessment in the light of all the facts obtained. He was no believer in spot diagnoses: he carried out exactly the same time-consuming laborious routine for an obvious mongol.

Gesell was an imposing figure. I regarded him as a shy man who was not easy to get to know. When he talked to one about the philosophy of development, much of what he said was difficult to follow, but among it were many brilliant and fascinating ideas.

Those who had been privileged to work under him will always feel a debt of gratitude to him for welcoming them into his team and really going out of his way to share with them his knowledge, experience, and philosophy.

ELIZABETH BOLTON, C.B.E., M.D.

The death of Miss Elizabeth Bolton on May 25 at the age of 82 breaks one of the few remaining links with the early history of the Royal Free Hospital School of Medicine, of which she was dean for 14 years.

Elizabeth Bolton was born in Leeds in 1878, the daughter of a Congregational minister. Educated at Stoneygate College, Leicester, and Bedford College for Women, she studied medicine at the London (Royal Free Hospital) School of Medicine for Women, graduating M.B., B.S. in 1904 and proceeding M.D. two years later. She served as house-surgeon and surgical registrar at the Royal Free Hospital and as surgeon to the Canning Town Medical Mission. She became consultant surgeon to the British Hospital for Mothers and Babies, and from 1910 to 1940 she was consultant surgeon to the Elizabeth Garrett Anderson Hospital. On her retirement from consultant practice she was appointed medical officer in charge of Emergency Medical Service beds at Oster House, St. Albans, until 1945. She was a member of the School council from 1926 until 1957, and a member of the Weekly Board of the Royal Free Hospital from 1937 to 1947, and she served as dean from 1931 to 1945. She then became president of the School from 1945 to 1957 and only resigned on the grounds of failing health. She was created C.B.E. in 1935, and three years later she was elected president of the Medical Women's Federation.

Professor RUTH E. M. BOWDEN writes: The above brief recital of Miss Bolton's achievements and offices gives little idea of the energy and punctiliousness that characterized all her work, and it can give no indication of her great humanity, which was the most valuable and lasting gift she gave to all those with whom she worked and to the students whom she trained.

Miss Bolton had first-hand knowledge of many of the pioneer women in her profession, and was saddened at times by the ease with which their work seemed to be forgotten. She had the highest regard for integrity and for those who fought their professional battles fairly, but held ruthless aggression in low esteem and described it as "horrid." She herself was forthright and fearless, gave no place to vain regrets, and expected us all to meet difficulties with her own courage and sense of proportion. The portrait by Mr. William Dring, R.A. (part of which is here reproduced), gives an insight into the strength and warmth of her character;

her humour and the accompanying twinkle in her eye are well seen. As dean she steered the Medical School through the stormy seas of the war. Preclinical students moved to Aberdeen and St. Andrews, back to London and on to Exeter, and back again to London; clinical students were scattered between London, Arlesey, and St. Albans. Miss Bolton travelled widely, at times in the utmost discomfort, to keep in touch with her staff and students. She managed to save much of the tradition and cohesion which many feared would be shipwrecked beyond reclaim. In her view it was necessary "to get on with things," and she set the example and managed to find it all "interesting." She was one of the casualties when the Medical School was hit by a V2 bomb in 1945. Characteristically she refused to go off duty until all the students were at work again some few days later in two of the other London schools whose ready response to our need was never forgotten.

A generous-minded woman who had an understanding appreciation of the rights of each individual could not fail to have friends, and these Miss Bolton found in every age group. She delighted in the company of children, whom she regarded as "sensible people"; their candour and lack of false respect of persons were prized. These endearing qualities were hers too, and her many friends will miss her warmth and kindness and absolute integrity.

H. L. ATTWATER, M.Ch., F.R.C.S.

Mr. H. L. Attwater, formerly senior surgeon at All Saints' Hospital—later All Saints' Urological Centre (Westminster Hospital)—died in London on May 22. He was 75 years of age.

Harry Lawrence Attwater was born on June 1, 1885, the son of a barrister. He won a scholarship to Merchant Taylors' School and an exhibition to Pembroke College, Cambridge. Going on to Guy's Hospital for his clinical training, he qualified in 1909, graduated M.B., B.Chir. in 1911, and proceeded M.Ch. in 1913, having been elected F.R.C.S. in the preceding year. After resident appointments at Guy's and the Westminster Hospital, he served in the R.A.M.C. throughout the first world war. On his return to civilian life he was appointed surgical registrar at All Saints' Hospital and then joined the late Mr. Edward Canny Ryall as his personal assistant. Appointed to the honorary staff of All Saints' Hospital 30 years or so ago he retired as senior surgeon in 1950 and became honorary consulting surgeon to the Westminster Hospital.

Over the years he became well known in Britain as a urological surgeon and was president of the Section of Urology of the Royal Society of Medicine in 1942. He was one of the original members of the committee which started the *British Journal of Urology* in 1929, and subsequently became its treasurer, an office he held until 1960. A Founder Member of the British Association of Urological Surgeons, he was also a member of the International Society of Urology. He served as president of the Hunterian Society in 1936–7.

Mr. Attwater was a reserved and scholarly man. He published a number of papers on his specialty in this and other journals and was the author of several chapters in Winsbury-White's *Textbook of Genito-urinary Surgery*. As a young man he was a mathematical scholar of some distinction, and he retained all his life his interest in numbers: the Pyramids of Egypt were always one of his absorbing interests.

Mr. Attwater was twice married. His first wife died in 1929, and in 1933 he married Doris Emily Winter, daughter of the late George Callaway, and she survives him.

R. G. ABERCROMBIE, M.D., D.T.M.

The death on May 14 of Dr. R. G. Abercrombie at the advanced age of 88 removed one who was for many years a familiar figure in many circles in Sheffield and closed a long and distinguished chapter of work in the teaching hospitals in the city.

Rodolph George Abercrombie, who was the brother of Sir Patrick Abercrombie, the famous architect, and Lascelles Abercrombie, the poet, was born on August 21, 1872. He studied medicine at Cambridge and at St. George's Hospital, qualifying in 1900, graduating M.B. in 1902, and proceeding M.D. in 1910. He worked first in Sheffield at one of the voluntary hospitals—the Royal Hospital—and from there he was appointed to a new venture in treatment when the Edgar Allen Institute for Medico-Physical Treatment was established in the summer of 1911. Mr. Edgar Allen, a Sheffield industrialist, started the project, having visited and become interested in the work of various centres in Europe and having explored the matter with the officers of the Sheffield Division of the British Medical Association, who also approved of the venture. Indeed, the then honorary secretary of the Division served for many years afterwards on the management committee of the Edgar Allen Institute. The methods used included not only massage, exercises, and heat treatment but also the extensive use of many and varied types of mechanical apparatus. Much of this treatment was at that time new in this country, and Abercrombie, having been appointed medical director of the Institute, spent some time abroad studying and learning the then most up-to-date methods in use.

On the outbreak of war in 1914 Abercrombie volunteered for service in the R.A.M.C. and served throughout the war, being over four years in France and Belgium—mostly with base hospitals, except for a short period with a field ambulance in 1918.

D. C. B. writes: I first met Abercrombie in 1917 when he was serving with No. 4 General Hospital on the coast in North France, and worked together with him for many months in a unit devoted to the care of cases of penetrating wounds of the chest. In the officers' mess, "R. G. A." was a popular member. His high intelligence and keen wit made him impetuous at times in thought and speech, so that some utterances led to regrets afterwards, but he was always a lively and co-operative member. Indeed, one can recall occasions when he was pressed into service in football and hockey teams for matches between the officers and hospital staff. After his war service he returned to Sheffield, and, besides continuing his work as medical director of the Physical Treatment Institute, was appointed assistant honorary physician to the Royal Hospital and for a short time was in private practice as a physician. Later he confined himself to the expanding work of the Edgar Allen Institute until retiring in 1949.

He remained a bachelor. Apart from his medical work, Abercrombie was always interested in the "out of doors" and in natural history. For some time he was chairman of the Sheffield and Peak District Branch of the Council for the Preservation of Rural England, and, for five years, also chairman of the Longshaw Management Committee of the National Trust, while his talks to the Sorby Natural History Society's members were always highly appreciated.

F. E. CHESTER-WILLIAMS, M.R.C.S., L.R.C.P. F.F.R.

Dr. F. E. Chester-Williams, medical director of the Bradford Regional Radium Institute, died suddenly at his home on May 12. He was 60 years of age.

Frank Edward Chester-Williams qualified M.R.C.S., L.R.C.P. from St. Bartholomew's Hospital in 1924. After holding various junior hospital appointments he was attracted to the radium treatment of disease, then in its infancy, and obtained the post of house-surgeon at the Radium Institute, where he remained for three years. In 1928 he was appointed physician in charge of the radium therapy department in Bradford Royal Infirmary, a department set up by the very progressive board of that institution and made possible by many generous benefactions. Armed with some £20,000, Chester-Williams himself travelled to Belgium to negotiate the purchase of the radium required and made all arrangements for its transport and storage. He set about designing a building to be used exclusively for treatment

by radium, this building to be incorporated in the new Infirmary then being erected. In 1943 it was completed, and he had the satisfaction of seeing a new Regional Radium Institute opened with himself as its medical director. As this Institute drew patients from a wide and populous area he held consultant posts in many surrounding hospitals, including those of consultant radiotherapist to the Royal Halifax Infirmary and to the Huddersfield Royal Infirmary.

Recognized as a pioneer in his specialty, he was made a founder Fellow of the Faculty of Radiologists in 1940 and for two years he served as a member of the council of that body. He was president of the British Institute of Radiology (Northern Section) for two years, the first radiotherapist to hold that office—a fact of which he was justifiably proud. In local medical affairs he took an active interest. He was chairman of the local Division of the B.M.A. and for eight years he was a member of the Radiologists Group Committee of the Association. For many years he was secretary of the Bradford Medico-Chirurgical Society. In 1942 he acted as question-master in a brains trust at the Faculty of Radiologists' annual meeting, where his flair for this type of work ensured the success of an interesting experiment.

Chester-Williams ran his institute with remarkable efficiency, achieving a bed-occupancy rate the envy of all his colleagues. His staff were devoted to him, although he drove them hard. Extremely conscientious himself, he was intolerant of slackness of any kind in others. Endowed with a cheerful and optimistic disposition, he was exceedingly popular among his patients, and, working in a field where prognosis was only too often unfavourable, this gave to them a confidence and hope which were invaluable. The very large attendance at his memorial service bore ample testimony to the respect and affection in which he was held by so many of them.

A good mixer, "Chester" had a host of friends. He was an admirable after-dinner speaker with a remarkable fund of stories, while his descriptions of amusing incidents in work or play, illustrated by much characteristic gesture, were always a delight. During his last years he suffered from an increasingly incapacitating illness which greatly reduced his activities, but he bore this with the courage and cheerfulness which all who knew him expected of him: he continued to work as he had always done, treating his disability with contempt. Indeed, he carried out his normal full day's work on the day before he died. In his home life he was especially fortunate, and many will greatly miss the happy and welcoming atmosphere of his sitting-room when they called to pass the time of day with this most amusing and lovable man. He leaves a widow and two sons.—J. K. R.

E. DOUGLAS GRANGER, M.D.

Dr. E. Douglas Granger, who had practised in Bournemouth for many years, died at his home there on May 3, aged 70.

Edmund Douglas Granger was born at Wimbledon on February 1, 1891, and was educated at King's College School, Wimbledon, and St. Thomas's Hospital. Qualifying in 1914, he joined the Royal Navy as a temporary surgeon, serving throughout the first world war and being present in H.M.S. *Centurion* at the Battle of Jutland. After the war he returned to St. Thomas's, where he held various posts, including those of house-physician and obstetric house-physician. In 1923 he came to Bournemouth and joined an old-established practice in which his brother Henry was a partner. In 1924 he married Miss Kathryn Jones, by whom he had two sons, both trained at St. Thomas's Hospital and now practising in Bournemouth, and also a daughter, who is married to Dr. T. M. Richards, of Haslemere, likewise a former student of St. Thomas's.

Dr. Douglas Granger entered very fully into the medical life of Bournemouth, being president of the Medical Society for two years. In the discussions which took place before the introduction of the National Health Service he was a prominent debater, urging the more gradual introduction of the Service. For recreation he enjoyed riding, and he hunted regularly once a week during the season. Mention must also be made of his daily bathe in the sea, summer and winter, before breakfast. This seemed to keep him remarkably fit.

Douglas Granger was a man much liked by his colleagues, for he had a great sense of loyalty. His innumerable patients testified to his most lovable character. Many since his death have written calling him their "beloved physician." He will be greatly missed by Bournemouth doctors, who send a message of sincere sympathy to his widow and family.—E. B.

Dr. C. K. J. HAMILTON writes: I first met Douglas Granger as a young house-physician. At that time he was courageously overcoming the after-effects of encephalitis, contracted while on active service in the Navy during the first world war. These sequelae indeed dogged him throughout his life, but he never complained. Typical of him, I well remember how, when a patient died in the ward under his care, he not only did what he could for the patient but also remembered to prescribe a sedative for the relatives. Kindness and courage were to me the two outstanding characteristics of Douglas Granger. He always did a little more than was strictly necessary for his patients, such as providing a domestic pet for a lonely woman. His physical courage was well displayed in the way that he rode to hounds, having taken up riding rather late in life. He overcame his difficulties, and later never turned his horse's head at any fence, no matter how forbidding. Other men may arise and follow in his footsteps, but there will never be another Douglas Granger. His was a unique and lovable character.

IAN B. CUMMINGS, L.R.C.P.&S.Ed.

Dr. Ian B. Cummings, who practised in Lanark for 35 years, died in hospital on March 15, aged 63.

After service in the first world war, Ian Bruce Cummings went into the pharmaceutical business with his father, but soon decided upon a medical career. He trained in Glasgow, qualifying in 1922. Coming to Lanark in 1926, he went into partnership with the late Dr. D. V. Maxwell Adam, and latterly with Dr. Robert Allan. A keen clinician, he was always intensely interested in his patients, and was often seen in the hospital visiting patients whom he had sent in for specialist treatment. He was on the staff of the William Smellie Memorial Hospital, Lanark, as an anaesthetist from its opening in the spring of 1948. He also held appointments as factory doctor, medical referee to the Ministry of Pensions, medical officer to the Smyllum Orphanage in Lanark, and for a term served on the board of management of the Southern Lanarkshire hospitals. Dr. Cummings's varied interests included model engineering, toast-mastering, of which he became area governor, the British Legion, the Boy Scouts' Association, and ambulance, nursing, and first-aid organizations. A year ago he was elected unopposed to the town council of Lanark.

By the death of Dr. Cummings the upper ward of Lanarkshire has lost a good friend, a public-spirited citizen, and a conscientious doctor. His untimely death is a sad blow to his many friends and patients, and our sympathy is extended to his widow.—M. D. B.

T. HAROLD PETITT, *M.C.*, M.B., Ch.B.

Dr. T. Harold Petitt, who was in general practice at Mount Albert, Auckland, New Zealand, for some 40 years, died in Auckland on April 10 at the age of 71. A life governor of the Royal Life Saving Society, he was the only New Zealander to hold the Service Cross, the society's highest award.

Thomas Harold Petitt was born at Nelson, New Zealand, on August 1, 1889, the son of a former mayor of the town,

and was educated at Nelson College and Otago University. He graduated M.B., Ch.B. from the University of New Zealand in 1913, and soon afterwards came to England, where he held the appointments of house-surgeon at the Royal Victoria and West Hants Hospital, Bournemouth, and house-physician at the General Infirmary at Leeds. He was at Leeds in 1914 when the first world war broke out, and immediately volunteered for the R.A.M.C. He took part in the Gallipoli landings, and then served in France for the rest of the war, the last two years with the New Zealand Medical Corps. For his services he was awarded the Military Cross. After the war he returned to New Zealand and settled in general practice at Mount Albert, becoming also honorary physician to the Karitane Hospital, Auckland, in 1922. For five years he was chairman of the board of governors of the hospital, to which he became ultimately consulting physician. He also served on the medical advisory board of the Plunket Society, and was for many years superintendent of the Mount Albert division of the St. John Ambulance Brigade, and for his work was appointed an officer in the Venerable Order of St. John of Jerusalem.

During the second world war he was in command of the 9th Field Ambulance for two years, later serving as an assistant director of medical services with the 2nd New Zealand Expeditionary Force in 1943, and as liaison officer in the Dutch hospital ship *Oranje* in 1945. After the war he went to Japan as senior medical officer with the 2nd New Zealand Expeditionary Force and as officer commanding the 6th New Zealand General Hospital. Subsequently he was assistant director of medical services for the Northern military district of New Zealand until 1950, in which year he was awarded the Efficiency Decoration.

Harold Petitt was a great sportsman. As a swimmer, he was champion of Nelson and Nelson College in 1907, and later in life became patron of the Auckland branch of the New Zealand Surf Life Saving Association. He also served on the National Council of Physical Welfare and Recreation. He had a world-wide reputation as a deep-sea angler, being president of the New Zealand Deep Sea Anglers' Association from its foundation, and the New Zealand representative on the International Game Fish Association.

Dr. Petitt leaves a widow. His brother, Dr. William H. Petitt, is in practice in Auckland.

E. R. WILLIS, M.R.C.S., L.R.C.P.

Dr. E. R. Willis, who formerly practised in Wellington, Somerset, died suddenly at his home there on April 18. He was 62.

Edward Rendle Willis served as an officer in the Royal Navy during the first world war, but later left the Navy to become a medical student at the London Hospital, for which he played Rugby football, also captaining the cricket eleven in 1925. After qualifying in 1930, he held a house appointment at the Taunton and Somerset Hospital before entering general practice at Wellington, where he became well known. In addition to being honorary secretary to the West Somerset Division of the B.M.A. in 1939 and from 1945 to 1948, he was chairman of the Division from 1950 to 1952. An example of the very best type of general practitioner, Dr. Willis enjoyed his work, and never spared himself; he had, therefore, the affection and gratitude of all his patients, to whom he was both kind and generous. When ill-health compelled him to retire three years ago, he was greatly missed by all.

He leaves a widow, one son, and two daughters.—L. P. M.

A. DICKSON STIRLING, D.S.O., M.B., Ch.B. D.P.H.

Brigadier A. Dickson Stirling, formerly deputy assistant director-general of Army Medical Services at the War Office, died in Edinburgh on May 2 at the age of 74.

Alexander Dickson Stirling was born at Arbroath, Forfarshire, on June 8, 1886, the second son of the Rev. Alexander Stirling. From the Arbroath High School he went on to University College, Dundee, to study medicine, and graduated M.B., Ch.B., with distinction, from St. Andrews University in 1907. Four years later he took the D.P.H. After graduation he held the appointments of house-physician and senior house-surgeon at Dundee Royal Infirmary before entering the R.A.M.C. in 1909. The early part of his Service career was spent in the United Kingdom, and from 1911 to 1914 he was in Egypt, being promoted captain in 1912. Soon after the outbreak of the first world war he was sent to France, where he served throughout the war, except for a very brief period in Italy in 1917. During the war he was four times mentioned in dispatches, awarded the D.S.O. in 1918, and appointed a Cavaleiro in the Portuguese Order of Avis in 1919. From the latter year until 1923 he was temporary deputy assistant director-general of Army Medical Services at the War Office, with the rank of major. He then spent some years in India, being deputy assistant director of medical services, Northern Command, from 1925 to 1928. He was deputy assistant director-general at the War Office from 1930 to 1934, and after further service in India he became full colonel in 1937. He was in Britain when the second world war broke out, and was immediately sent to France as a deputy director of medical services, returning at the time of the evacuation in 1940. Soon afterwards he was again mentioned in dispatches in recognition of distinguished services rendered in connexion with operations in the field. He served at home from 1940 to 1944, and in North-West Europe until the end of hostilities. Promoted acting brigadier in 1940 and temporary brigadier in 1941, when he retired from the Army in 1945 he was granted the honorary rank of brigadier.

Dickson Stirling was a member of the War Office committee on shell shock, of which the first Lord Southborough was chairman. Over a long period of time he was a member of the permanent committee of the International Congress of Military Medicine and Pharmacy, and was honorary secretary of the fifth international congress held at B.M.A. House, London, in 1929. Always a keen and conscientious officer, he performed the onerous duties of the secretary of the congress with outstanding success.

In 1925 he married Miss Isobel Matthew, and she survives him. There were two sons and two daughters of the marriage.

D. CALWELL, M.B., B.Ch.

Dr. D. Calwell, who was a general practitioner in Belfast for nearly 50 years, died suddenly in Whitehead, Co. Antrim, on May 7. He was 72 years of age.

David Calwell was born in Belfast in 1888, the youngest of a large family of which five members (four brothers and a sister) entered the medical profession and were engaged in general practice in Belfast at the same time. He studied medicine at Queen's University, graduating M.B., B.Ch. in 1913. A few months after qualification he put up his plate in a densely populated factory area of Belfast, continuing to practise in the same house until his death. In spite of failing health he was actively engaged in the work of the practice (along with his younger son) until the end, and on the day of his death he conducted the morning surgery.

Some years ago a group of general practitioners in north Belfast of which he was chairman paid him the compliment of commissioning his portrait and presenting it to him in recognition of his services to his medical colleagues in the district. An active member of the British Medical Association, he was a member of the Northern Ireland Branch Council for many years. His wise counsel, based on a lifetime's experience in the practice of medicine, will be greatly missed. Held high in the affection and esteem of his patients and colleagues in all branches of the profession, he went well beyond the bounds of ordinary professional care, sharing wholeheartedly whatever other troubles the family whose doctor and friend he was might be facing. He was accustomed to prescribe and dispense unusual treatments such as a gift of money or turkey and plum pudding from

his own Christmas dinner table or a holiday in his house at the seaside in cases where he thought these were indicated. Such extrapharmacopoeial remedies were an integral part of his equipment, and he used them without any air of charity or patronage.

If Dr. Calwell had not entered the medical profession he would have made a good farmer. He had an abiding interest in the land and sometimes spoke as if he had abandoned his rightful vocation by following his elder brothers and his sister into medicine. As it was, he found a good substitute in the garden at his seaside home, and he derived much pleasure from growing fruit and vegetables and perhaps even more pleasure in distributing them to his friends.

He is survived by his widow and three children. His elder son is a teacher of biology, his younger son was his partner in the practice, and his daughter is also a member of the medical profession.

S. K. HUTTON, M.D., D.Obst.R.C.O.G.

Dr. S. K. Hutton, who was a medical missionary in Labrador before the first world war and later became honorary secretary of Moravian Missions, died on May 11 after a road accident. He was 83 years of age.

Samuel King Hutton was born at Kilkeel, in County Down, on November 26, 1877, his father being a minister of the Moravian Church. From Manchester Grammar School he went on to study medicine at Owens College, graduating M.B., Ch.B. in 1900, and winning the medal for operative surgery. After holding the posts of house-physician and house-surgeon at Ancoats Hospital and taking the Certificate in Tropical Diseases of the University of Liverpool, he was called as a doctor to Okak, a little village settled by the Moravian Mission on the bleak coast of Labrador. Ill-health brought him back to Britain in 1913, and he settled in practice at Poole in Dorset, becoming honorary surgeon and gynaecologist to the Cornelia and East Dorset Hospital. During the first world war he served in France as a captain in the R.A.M.C.

Leaving Poole in 1928 he went into practice at Orpington, Kent, remaining there until his retirement to Bridgwater in Somerset 10 years ago. He proceeded to the degree of M.D. of Manchester in 1925 and took the D.Obst.R.C.O.G. in 1935. He continued all his life to work for the Moravian Church in one capacity or another.

E. W. writes: Dr. Hutton had great literary gifts and published a number of books on life in Labrador, while for many years editing the Moravian missionary paper. For the last 24 years he worked on the Eskimo textbook, translating into Eskimo the daily texts and readings used by the Moravian Church all over the world. A man of deep evangelical convictions, he represented the Moravian Church on the Evangelical Alliance for many years, and also served on the committee of the London Association in aid of Moravian Missions, an interdenominational body which raises considerable funds every year for Moravian Missions. Dr. Hutton was one of seven delegates elected to represent the British Province of the Moravian Church at a General Synod held in America in 1957, when matters of concern to the world-wide Moravian Church were decided. The same gifts which made his writings so warm and personal made him also a most acceptable and interesting speaker, and he loved nothing better than to have some opportunity of speaking of his faith in his Lord, and of the missionary work of the Moravian Church.

HAMILTON BAILEY, F.R.C.S., F.A.C.S.

The obituary of Mr. Hamilton Bailey was published in the *Journal* of April 8 (p. 1043).

Mr. CHARLES MACMILLAN, chairman and managing director of E. and S. Livingstone Ltd., writes: In all the obituary notices relating to Hamilton Bailey one point has been overlooked. Special praise is due to him for his great pioneering work in illustrating British textbooks. To-day many teaching hospitals and university departments have medical artists and departments of photography, but before the advent of Hamilton Bailey's classic publication *Physical Signs in Clinical Surgery* the illustrations in British textbooks were very poor. Many British authors have "gifted pens," but 30 years ago British publishers had much to learn from their American colleagues in the art of medical pictures.

Hamilton Bailey gloried in beautiful illustrations. His belief was that "a thing of beauty is a joy for ever" regardless of the difficulty and expense incurred in preparing such. No one will ever know how much time and money he expended to ensure that every book with which he was associated had the stamp of his perfection on it. Many authors have informed me that they were inspired by his example to be satisfied only with the very best illustration material possible. It will always be a great tribute to a great master—Hamilton Bailey—that the quality of illustrations in British textbooks is now of the highest possible standard. All honour to his noble lead.

Dr. E. J. C. HAMP writes: As an Australian who knew the late Mr. Hamilton Bailey well I would like to pay a tribute to him. No name in the field of surgery was so well and favourably known to so many, for there could scarcely be a medical graduate anywhere in the British Commonwealth of Nations who has not profited by studying his several books. Hamilton Bailey has stood out predominantly as a great teacher of surgery. His rare gift for lucid writing enabled him to present a multiplicity of surgical subjects so clearly that his books became the most sought-after of all texts in the field of general surgery. He was for ever searching for more and better diagrams and wider scope, so that each new volume was larger and more informative than its predecessors. Much of his time was spent in scanning world literature so that he could keep up to date with modern thought and practice. There are many doctors situated in out-of-the-way places who come up against surgical emergencies of a kind with which they are unfamiliar. Hamilton Bailey's *Emergency Surgery* must have been consulted countless numbers of times by such doctors. The number of individuals who owe their lives to knowledge so gained must be inestimable. Hamilton Bailey was very much an individualist in days when individualism is fast fading. His associations with so many giants of the past from so many nations linked him between old and new. His life was devoted to the cause of surgery, and very successfully. Without the help and co-operation of his wife, Mrs. Veta Bailey, it is doubtful if he could have reached such heights of fame and usefulness. A better combination it would be hard to imagine.

Sir HUGH GRIFFITHS, C.B.E., M.S., F.R.C.S.

The obituary of Sir Hugh Griffiths was published in the *Journal* of May 27 (p. 1545).

G. R. F. writes: I came to know Sir Hugh Griffiths well during the last seven years of his appointment at the Albert Dock Hospital before his retirement in 1956. No young consultant could have had a kinder or more loyal senior colleague. He was a man of shrewd and rapid judgment and once given the facts he could come to a decision with charm and ready wit. He could not abide the second-rate and he would not hesitate to take appropriate action if he felt that the patient's welfare was in jeopardy. His knowledge of injury in relation to function was truly encyclopaedic, and it is to be regretted that he was not able to leave a more permanent record of a lifetime's observations. The Albert Dock Hospital was the consummation of his pioneering efforts, and we who were associated with him are proud to continue the great traditions which he established there.

Medico-Legal

ADVERTISING BY COSMETIC PLASTIC SURGEON

APPEAL REJECTED BY PRIVY COUNCIL COMMITTEE

On May 31 Lord MORRIS OF BORTH-Y-GEST delivered the judgment of the Judicial Committee of the Privy Council on the appeal by Mr. LESLIE ELGAR GARDINER, of Wimpole Street, from an order of the General Medical Council on May 25, 1960, directing that his name be erased from the *Medical Register* (*Supplement*, June 11, 1960, p. 364). The appeal was before Lord TUCKER, Lord DENNING, and Lord MORRIS OF BORTH-Y-GEST. Mr. Gardiner appeared in person, and Mr. Peter Boydell and Mr. Hugh Carlisle for the General Medical Council.

JUDGMENT

Lord MORRIS OF BORTH-Y-GEST said that the appellant, a qualified medical practitioner, who was registered under the Medical Acts, had appeared before the Disciplinary Committee of the General Medical Council on a charge of "infamous conduct in a professional respect." It was alleged that he had advertised for the purpose of obtaining patients or promoting his own professional advantage. This it was said he had done in four ways as follows:

"(1) By writing for publication and causing to be published in 1959 a book entitled *Faces, Figures, and Feelings* which included matter directing attention to your professional skill, knowledge, services and qualifications.

"(2) By sanctioning or acquiescing in the publication in the issue of the *Sunday Pictorial* dated December 13, 1959, of an article entitled 'This Man Makes Faces' which purported to be based on an interview given by you and which included matter directing attention to your professional skill, knowledge, services, and qualifications.

"(3) By sanctioning or acquiescing in the publication in the issue of *Woman* dated February 20, 1960, of an article entitled 'Leslie E. Gardiner, Cosmetic Plastic Surgeon,' which included matter directing attention to your professional skill, knowledge, services, and qualifications.

"(4) By procuring or sanctioning the publication in the issues of *Woman* dated February 27, March 5, March 12, March 19, and March 26, 1960, of a series of articles entitled 'Cosmetic Plastic Surgeon' of which you were stated to be the author, and which included matter directing attention to your professional skill, knowledge, services, and qualifications."

After inquiry the Disciplinary Committee had determined that the facts alleged against him under (2) above had not been proved to their satisfaction but had determined that the facts alleged against him under (1), (3), and (4) above had been proved to their satisfaction. On the basis of those findings they had judged him to have been guilty of "infamous conduct in a professional respect" and had directed the Registrar to erase his name from the *Register*.

Pursuant to section 36 of the Medical Act, 1956, Mr. Gardiner now appealed. It was provided by section 33 (1) (b) of the Medical Act, 1956, as follows: "If any fully registered person . . . (b) after due inquiry is judged by the Disciplinary Committee to have been guilty of infamous conduct in any professional respect, the Committee may if they think fit direct his name to be erased from the *Register*."

Matter to be Decided

It became necessary to consider whether the actions of the appellant could fairly and properly be regarded as amounting to advertising for the purpose of obtaining patients for himself or for the purpose of promoting his own professional advantage: if so whether he was guilty of "infamous conduct in a professional respect": and if so whether the Committee were right in directing the erasure of his name from the *Register*.

The appellant had practised for many years as a consultant ear, nose, and throat surgeon. For the last nine or ten years he had also practised what had been called "cosmetic surgery." In essence this branch of surgery was concerned to alter and to improve certain naturally existing personal physical features. It might be contrasted with what had been called "plastic surgery," which in general was concerned to ameliorate or correct physical distortions resulting from injuries or accidents either in war or in peace. The appellant described the scope of his work as a cosmetic plastic surgeon as including "the alteration first of all of the shape of people's noses, the removal of wrinkles round their eyes, the removal of bags under their eyes, what is commonly called face-lifting, and also the reduction of the large breasts that women suffer from and sometimes the making of small breasts larger."

Articles in "Woman"

The appellant had written a book entitled *Faces, Figures, and Feelings*, and made an agreement with publishers dated January 9, 1959, for its publication. The book was actually published in December, 1959. He had been advised to employ literary agents in connexion with the publication. His agents had made a contract in about the month of September, 1959, for the publication in a magazine called *Woman* of certain weekly articles which were said to be by way of serialization of the book. The magazine in question was proclaimed on its cover to be the "World's Greatest Weekly for Women." The appellant gave permission for the articles to be published. The various articles appeared in the issues dated February 27, March 5, March 12, March 19, March 26, 1960. In the issue of the magazine dated February 20 there appeared an article which was designed to direct the attention of readers to the articles which were to follow in subsequent weekly issues and to create and stimulate an interest in respect of them in the readers of the magazine. That article had included a photograph of the appellant. The article was not written by the appellant but by one of the staff writers of the magazine.

The appellant saw a galley-proof of the article of February 20, and made a request that his photograph should not be included. It was, however, the wish and the decision of the magazine that it should be. In the articles themselves there were some photographs which illustrated operations. The appellant did not appear in these. There were photographs of the appellant at the head of the articles: these were printed from a photograph supplied by the appellant. The weekly articles themselves were founded upon and as to their substance matter were in the main closely drawn from the book, but in some instances the accounts or descriptions of incidents were adapted and embellished. A few rather arresting passages in the articles had no origins at all in the book. It was said that certain human or personal notes had been introduced in order to make the theme acceptable to the general reader. The penmanship or authorship of the articles was not that of the appellant, but galley-proofs of the articles were sent to him and he approved them. He received payment for the articles.

Contents of Book

The book itself, which their Lordships had deemed it desirable to read, contained an autobiographical account of the appellant's life and career, described how he came to be concerned with cosmetic surgery, explained the nature of such surgery, and gave accounts of very many successful operations performed by the appellant. The book might fairly be said to proclaim that there need be no prejudice against cosmetic surgery or ignorance in regard to it, that it might be resorted to without fear, and that the appellant was one who by his training, his skill, and his experience had brought relief and happiness to his patients. Inside the book following the title "Faces, Figures, and Feelings"

were the words: "A Cosmetic Plastic Surgeon Speaks by Leslie E. Gardiner, F.I.C.S., M.R.C.S., L.R.C.P., D.L.O." The cover or wrapper of the book set out an explanation of the scope of the work in the following terms:

"Cosmetic Plastic Surgery: what is it—face-lifts, altering the shape of ears and noses, remoulding women's breasts? Is it the step-child of plastic surgery, rather hushed up, or is it practised undercover by quacks?

"Leslie Elgar Gardiner here tells the intriguing story of how he crossed the frontiers of his own orthodox speciality of ear, nose, and throat surgery into a fascinating world which, to many doctors and members of the public, suggests unorthodoxy. He dispels the legend of wickedness. The majority of his patients are neither ageing duchesses nor vanity-ridden members of the entertainment world. They are ordinary people, burdened by personal problems to which they want an answer.

"He tells how he felt the compelling challenge of a new kind of work that called for precision, delicacy, and skill. In America and on the Continent, where cosmetic plastic surgery is regarded as a speciality in its own right, he pursued his studies and witnessed the work of many distinguished surgeons in this field.

"He explains in the simplest terms how cosmetic plastic operations are done; and reveals through numberless case-histories the human beings who consult him and why.

"He is the first British plastic surgeon ever to do this. His book is illustrated with remarkable real-life case photographs and sketches that show vividly just what cosmetic plastic surgery can do. The book is a 'must' for every man and woman who wishes to know, not what cosmetic plastic surgery is rumoured to be, but what it is."

Their Lordships' Approach

On another part of the wrapper there was a biographical note (with a photograph) concerning the author. The appellant had been persuaded to allow his photograph to appear. Their Lordships proposed to approach the case by considering whether the contents of the book could be regarded as making its publication objectionable, and on the basis that the form and style of this part of the wrapper would not alone render it so.

The charge that the appellant was called upon to meet had been thus expressed: "that you have advertised for the purpose of obtaining patients or promoting your own professional advantage." It was to be noted that the particulars did not refer solely to the fact that the book and the articles had been published but that they "included matter directing attention to your professional skill, knowledge, services, and qualifications." It had therefore been necessary for the General Medical Council, and on appeal it was necessary for their Lordships, to consider the nature of the written material, the mode of publication which had been adopted, and all the circumstances relating to the purposes and reasons which had inspired the publication.

It must be recognized that professional medical men might be amply justified in publishing books and articles and in publishing them in their own names. By their writings they might be making invaluable contributions to medical science and to learning. They might be disseminating useful knowledge. They might be helping their fellow practitioners. They might be advantaging a wider public. It must, however, be recognized that by their writing they might inevitably and indeed justifiably attract notice. This might redound to their professional and to their pecuniary advantage. It might well be that in some cases a hope that some legitimate meed of personal advancement would result might find its place amongst the motives in writing, and might be the spur to command the industry that the task might require. But after this had been said it could definitely be said that within the profession the line between the kind of publication that was unobjectionable and the kind that was objectionable should present no difficulties of recognition for any reasonable practitioner. The accepted ethical standards of a profession might not be formulated in any written code and might not have found expression with the precision of language associated with a code, but yet they were quite clearly within the comprehension of qualified and experienced members of the profession.

"Warning Notice"

It might be noted that it had been the practice of the Medical Disciplinary Committee to issue what was called a "Warning Notice" for the Guidance of Registered and Provisionally Registered Medical Practitioners. The appellant had received a copy of such notice on May 19, 1954. The notice contained the following:

"(6) Advertising and Canvassing

The practices by a registered medical practitioner:

(*a*) Of advertising, whether directly or indirectly, for the purpose of obtaining patients or promoting his own professional advantage; or, for any other purpose, of procuring or sanctioning, or acquiescing in, the publication of notices commending or directing attention to the practitioner's professional skill, knowledge, services, or qualifications, or depreciating those of others; or of being associated with, or employed by, those who procure or sanction such advertising or publication; and

(*b*) Of canvassing, or employing any agent or canvasser, for the purpose of obtaining patients; or of sanctioning, or of being associated with or employed by those who sanction, such employment,

are in the opinion of the Committee contrary to the public interest and discreditable to the profession of medicine, and any registered medical practitioner who resorts to any such practice renders himself liable, on proof of the facts to the satisfaction of the Committee, to have his name erased from the *Register*."

The published warning against advertising, either directly or indirectly, for the purpose of obtaining patients or of promoting personal professional advantage was therefore clear.

Examples of What is Allowable

Examples might be given. On the one side of the line there might be a book or an article which was an exposition of a particular subject either written as a textbook for medical students or practitioners or written impersonally in order to give information to the general public. No exception could be taken to such publication. As an example on the other side of the line there might be a book or an article an essential theme of which was the praise and commendation of the skill and abilities of the writer himself, with an express or implied suggestion that his successes in dealing with cases showed that potential patients would do well to have recourse to him. That would be "advertising."

It might be entirely proper in the case of a book or article which was written impersonally as an exposition of a medical subject or to convey valuable general advice not only that the name of the writer should appear but that, possibly on a wrapper, there should be some factual mention of his position and attainments; the authority of the exposition might thereby be shown. But this would be in contrast to a book or article which was written in the hope and with the purpose of attracting patients and increasing a practice; for that would be self-advertisement to which exception could properly be taken.

Self-advertisement

There did not appear to be any doubt that the medical profession condemned self-advertisement. In his judgment in *Rex* v. *General Medical Council* [1930] 1 K.B. 562 Scrutton, L.J. (at page 569), had recognized that in the medical profession advertising might amount to serious misconduct in a professional respect. He had added that serious misconduct judged according to the rules, written or unwritten, governing the profession was denoted by the phrase "infamous conduct." In *Allinson* v. *General Council of Medical Education and Registration* [1894] 1 Q.B. 750 one question which had arisen was whether there was evidence upon which the Council could reasonably find that the plaintiff had been guilty of "infamous conduct in a professional respect." In his judgment Lord Esher, M.R., said (at page 760):

"Was there, then, any evidence which justified the Council in finding the plaintiff guilty of 'infamous conduct in a professional respect'? I adopt the definition which my brother Lopes has

drawn up of at any rate one kind of conduct amounting to 'infamous conduct in a professional respect,' viz.: 'If it is shewn that a medical man, in the pursuit of his profession, has done something with regard to it which would be reasonably regarded as disgraceful or dishonourable by his professional brethren of good repute and competency,' then it is open to the General Medical Council to say that he has been guilty of 'infamous conduct in a professional respect.' The question is, not merely whether what a medical man has done would be an infamous thing for any one else to do, but whether it is infamous for a medical man to do. An act done by a medical man may be 'infamous,' though the same act done by anyone else would not be infamous; but, on the other hand, an act which is not done 'in a professional respect' does not come within this section. There may be some acts which, although they would not be infamous in any other person, yet if they are done by a medical man in relation to his profession, that is, with regard either to his patients or to his professional brethren, may be fairly considered 'infamous conduct in a professional respect,' and such acts would, I think, come within section 29."

That was a reference to section 29 of the Medical Act of 1858.

Davey, L.J., in his judgment at page 766, had said:

"The question is not whether the plaintiff is right or wrong in his views on the subject of medicine and hygiene. He may be right, notwithstanding his differences from the majority of his professional brethren. He may be in the position of Athanasius contra mundum. But there are different modes of stating one's opinions and views, and a man may be actuated by different motives in enforcing his views and opinions upon the world. In the present case the language in which the plaintiff has thought fit to express his views, and the circumstances under which and the surroundings with which his advertisements were issued, coupled with the notices to which our attention has been drawn, recommending his own works and his own advice, seem to me, when taken together, to be evidence from which the Medical Council might reasonably hold that his conduct was 'infamous in a professional respect.'"

In that particular case the plaintiff had been in the habit of inserting advertisements in newspapers in which his name and address were stated. These advertisements had contained reflections upon medical men generally and their methods of treating their patients, and had advised the public to have nothing to do with them or their drugs. The advertisements had contained a series of answers to real or imaginary correspondents as to the proper treatment of different complaints and there had been recommendations to apply to the plaintiff for advice, the amount of the fee charged by him for advice being stated. Certain works on medical subjects written by the plaintiff had also been mentioned and their prices.

Purposes of Book

It must be recognized that a book or an article might be written for more purposes than one. At the hearing before the Disciplinary Committee the appellant had been asked what his purpose was in writing his book. Certain answers and questions had followed:

"A. When I began to become interested in the work of cosmetic surgery the thing that struck me at the very beginning was how little people knew about it. In the very beginning, I, as a doctor, as an ear, nose, and throat surgeon, did not, for example, for some time—it did not dawn upon me that people wanted the shape of their noses altered, and then when I went into the matter more fully I discovered that even the ordinary, average general practitioner knew nothing about it and the public knew nothing much about it, and after some years in the practice of this speciality I realized that it was time that somebody did write a book about this, somebody with authority. I apologize if I should say that I am an authority, but somebody who had some experience in this work should write and for the first time put before the public what can be done and also inform the general practitioner about it as well.

"Q. Your book, then, was directed to the public at large and to the general practitioner.

"A. Yes.

"Q. With the object of informing them what could be done?

"A. Yes.

"Q. Was there a third object?

"Yes, there was a third object, because through a very odd tradition—I don't quite know if I am putting it in the best possible way, but a nucleus, a syndicate of certain men was fostering subversive propaganda among the public that this syndicate, of eight or nine people if you wish, were the only accredited people that could do this work. Now . . ."

Association of Plastic Surgeons

The appellant had proceeded to refer to an article which appeared in 1954 in a certain women's journal in regard to plastic surgery and which mentioned an Association of Plastic Surgeons. The appellant had said that he was disturbed to find that that Association were recommending the surgeons of certain teaching hospitals and no one else: it seemed, he had said, that a certain group were assuming that they were the only ones who could undertake plastic surgery. The article in question began as follows:

"In an age of many wonders, perhaps one of the greatest of them is plastic surgery. With the experience gained from the miracles of skin grafting and surgery done during the war, plastic surgery is now very far advanced. It is a branch of medicine about which everyone should know some of the details, so that they can appreciate its possibilities. It is not only surgery, it is an art which, when practised by skilled hands, performs marvels of transformation.

"Being out of the ordinary run of surgery, it is a profession which inevitably attracts charlatans. There is no law to prevent any man setting up as a plastic surgeon, but if anything untoward happens the patient has no redress. In any case, it is very necessary to be sure you have the services of a qualified man. Anyone can find out the qualifications of a surgeon by applying to the British Association of Plastic Surgeons, c/o Royal College of Surgeons, London W.C.2. Your own doctor should also be able to recommend a good plastic man or you can find one at most of the big hospitals."

In reference to this there had been the following question and answer:

"Q. In what way was your book going to help with regard to the attitude taken up by the association called the British Association of Plastic Surgeons?

"A. Well, the only way I think it could help, it would at least show that other sort of people than members of this association were just as well qualified to do this work as they were."

It was apparent therefore that the appellant had been saying in his evidence that he had more than one purpose in writing. In this connexion it might be observed that among the questions put to him by members of the Disciplinary Committee had been the following:

"Q. Did you realize that as a result of the publication of this book and of these articles in *Woman* you were likely to attract a number of people to you for your services?

"A. It was obvious, if anybody writes a book—it is an obvious question—yes.

"Q. Did you hope you would?

"A. Not particularly. I had enough practice."

Charge Unseverable

During the address of the appellant's counsel to the Disciplinary Committee the Legal Assessor had said that he would advise the Committee that in considering the charge it would not be enough for them to find merely that the appellant advertised but, inasmuch as the charge was unseverable, that they would have to decide whether the appellant advertised for the purpose of obtaining patients or promoting his own professional advantage: he had said that the Committee need not be satisfied that such a purpose was the exclusive purpose but that if the Committee were satisfied that the appellant advertised and that among his purposes there was to a substantial extent the purpose of obtaining patients or promoting his own professional advantage then it would be open to them to find the facts proved.

Their Lordships recognized that, while in some cases a particular purpose might be exclusive, there might be cases in which a particular purpose existed to a substantial extent and others in which a particular purpose was merely incidental, and it seemed to them that in finding that the facts alleged against the appellant under heads (1), (3), and (4) of the charge had been proved the Committee must be

taken to have held that in publishing his book and in sanctioning the publication of the articles the appellant had to a substantial extent the purpose of obtaining patients or promoting his own professional advantage. That had been their conclusion after a consideration of all the facts and after hearing the full evidence of the appellant and after hearing him examined and cross-examined.

B.M.A. Publications

On the appeal to their Lordships' Board (as to the nature of the appeal see *Fox* v. *General Medical Council* [1960] 1 W.L.R. 1017 and *Felix* v. *General Dental Council* [1960] A.C. 704) their Lordships had been fully referred to all the evidence and to the book and to the various articles in the magazine *Woman*. All the material had been the subject of careful analysis in the addresses of the appellant and learned counsel. At the request of the appellant certain other publications, including many issued under the sponsorship of the British Medical Association, had been considered by their Lordships. The appellant had referred also to certain press articles and to interviews as recorded in the press. Their Lordships had also been referred to the biographical and commendatory notes with photographs appearing on the backs of certain books written for laymen on medical subjects by medical men for a well-known popular series of books. The appellant had referred to some of these as denoting what he submitted that he was entitled to regard as legitimate conduct in medical men of good repute and competence. Their Lordships were not called upon to express any opinion in regard to any other book or article or in regard to any newspaper report of interview, but they had noted certain manifest contrasts between such of the publications containing medical advice as had been seen by their Lordships and the book written by the appellant together with the articles in *Woman*.

Appellant's Submissions

The appellant had submitted that the only facts that could properly be found by the Disciplinary Committee were that he had written the book and caused it to be published, and that he had acquiesced in the publication of the various articles in *Woman*, and that the conclusions of the Disciplinary Committee as to advertising represented inferences from these facts and that such inferences being open to review should be held to have been unwarranted and unjustifiable.

The appellant had testified in his evidence that one of his purposes in writing his book was to dispel and terminate a certain veil of secrecy which he said had shrouded cosmetic surgery, a secrecy which had had the result that no one had had the courage "to stand out in the open and say what it is" or to call himself a cosmetic surgeon. Another of his purposes had been to combat the "subversive propaganda" that the eight or nine members of a syndicate were the only accredited people that could operate, and to show that others were just as well qualified to do the work.

No Error in Decision

Their Lordships considered that the Disciplinary Committee were entitled to decide that in carrying out these purposes as acknowledged by the appellant himself he had had the essential purpose of presenting himself and his subject to the public and proclaiming himself as a cosmetic surgeon whose services (of the nature described by him in his book by reference to the many operations that he had successfully performed) the public might be well advised to seek. This would have furnished ample warrant for the conclusion that the appellant had to a substantial extent the purpose of obtaining patients or of promoting his own professional advantage. But quite apart from this the Committee were entitled to have regard to the content of the written material, the form in which it had been written, and the selected media for its publication in forming conclusions as to what had been the purposes which animated the writer. The Committee were entitled to consider whether a desire to give information about a subject and to direct attention to such a subject could have been achieved without directing attention to the personal and unique performances and abilities of the writer. Having been fully referred to the evidence and to the various articles in the magazine *Woman*, and having considered the book, their Lordships considered that there was ample material which warranted the decision of the Disciplinary Committee, and their Lordships saw no error in such decision.

Following upon their decision it had been open to the Committee to direct the erasure of the appellant's name from the *Register*, and it had been open to them not so to direct. If there was erasure an application for the restoration of a name to the *Register* might be made after a period of 11 months. (See Medical Act, 1956, section 34.) The Disciplinary Committee had considered it fitting to direct erasure. Their Lordships found no reason to think that in deciding to direct erasure the Disciplinary Committee had erred in principle or that their decision was unjustifiable. Accordingly their Lordships would humbly advise Her Majesty that the appeal should be dismissed. The appellant must pay the costs of the hearing before their Lordships' Board.

Medical Notes in Parliament

RATING OF LEARNED SOCIETIES

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The claim of the learned societies for relief from rating burdens which the Rating and Valuation Bill would impose on them was carried forward from the Commons to the Lords when the Bill came before the Upper House on second reading on May 31. Two clauses of the Bill give substantial effect to the recommendations of the Pritchard Committee on the rating of charities and kindred bodies. These were that property occupied by charities should receive 50% relief as of right, and that local authorities should have discretion to reduce or remit the remaining 50%; and that the Scientific Societies Act of 1843 (which gave exemption to societies for science, literature, and the fine arts) should be repealed.

Lines of Communication of Scientific Community

The Earl of HALSBURY, the principal spokesman for the learned societies, in a simple analogy, said that for the Government to spend more money on the scientific edifice and at the same time to prejudice the scientific societies was like extending a house at considerable cost and then ripping out the telephone wires so that nobody inside could communicate with anybody else. That was what the scientific societies did: they were responsible for the lines of communication of the scientific community. In addition to material relief, he also wanted greater certainty about how the future rating system was to be construed, and advocated a definition of exempt societies, with the Minister having power to schedule such societies after consultation with an advisory committee composed of representatives of scientific bodies. The societies would thus be judged by their peers on the basis of what they were doing, rather than by lawyers on the basis of what their memoranda and articles of association gave them power to do.

Subsidy from Westminster Ratepayers

Against this, the point was made that, desirable as the remissions might be, they really meant a subsidy from other ratepayers. Lord DOUGLAS OF BARLOCH put it directly: "I do not see a strictly logical reason why the ratepayers of Westminster should be called upon to support these bodies. Although they should be supported by some method or other, I doubt whether this is the right method." The

Earl of CRANBROOK, who spoke about a "disaster" if the ancient and important scientific societies were forced to cut down on their publications and libraries—the working tools of scientists—seemed to think a solution might be found if the decision were to rest with a county council rather than the smaller rating authority.

Lord Hailsham Offers Negotiation

What the Earl of HALSBURY asked from the Government was some positive assurance, as distinct from an expression of hope, about what they intended to do for the learned societies. All he got from Viscount HAILSHAM as the Government spokesman was the hope without the assurance. "On the whole," he said, "there is a prospect—I cannot give positive assurances to-day—of fairly general agreement between the Government and the societies about the way in which this should be tackled." He acknowledged that the Pritchard proposals had not met with the approval of Westminster and St. Marylebone, among other local authorities; he recognized what the burden of rates would mean to a society of this kind; and he had told a deputation from the learned societies, he recalled, that the Government were prepared to consider ways in which they could help. "My own thought is," he said, "that it cannot be dealt with by rate relief in any form; and if it is dealt with at all it will have to be by grants in some form." He nominated the royal societies and the British Academy as the best vehicles for this kind of negotiation, and left an open invitation for them to do so—"if they were prepared to act we should be glad to hear from them."

QUESTIONS IN THE COMMONS

Intake of Medical Students

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Minister of Health on June 5 whether he was reviewing, in the light of the current and future needs of the National Health Service, the conclusions of the Willink Committee on the intake of medical students, and if he would make a statement on future policy in this respect. Mr. ENOCH POWELL: The Secretary of State for Scotland and I are reviewing the data and calculations which underlie the estimates in the Willink Committee's Report. The student intake is larger now than when the committee reported. Mr. ROBINSON said he was glad to hear that, and, after describing the Willink Report as "one of the most disastrous ever acted upon," asked if they were not facing an increasing shortage of doctors. Mr. POWELL: So far from there being a reduction in the student intake following the Willink Report, the intake is higher than four years ago.

Dr. BARNETT STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister to agree that if the young registrars from the Commonwealth were to be withdrawn, as they might be in great numbers in future, there would be very great difficulty. Mr. POWELL said he agreed that that was an important factor in the statistical picture.

Dr. DONALD JOHNSON (Carlisle, Con.) asked the Chancellor of the Exchequer if he would state the number of students entering medical schools in each year for the last eight years. Sir EDWARD BOYLE said that figures up to 1953 were not available. Figures for the last seven years supplied by the University Grants Committee were as follows: 1954, 2,609; 1955, 2,700; 1956, 2,441; 1957, 2,497; 1958, 2,353; 1959, 2,472; and 1960, 2,580.

Doctors on Unemployment Benefit

Dr. DONALD JOHNSON asked the Minister of Pensions and National Insurance how many doctors were in receipt of unemployment benefit at the latest convenient date. Mr. J. BOYD-CARPENTER said he was informed by the Minister of Labour that on June 1, 1961, there were 30 doctors on the Professional and Executive Register in receipt of unemployment benefit.

Prescription Charges

Mr. L. PAVITT (Willesden, West, Lab.) asked the Minister of Health if he would reconsider the amount charged for items of prescription in the light of the 20% decrease shown by the fall from 22,200,000 items in February, 1961, to 17,500,000 items in March, 1961. Mr. POWELL: No. Mr. PAVITT claimed that this was adequate evidence of the failure of the policy on prescription charges. He also said he had submitted evidence to the Minister from the Willesden area of a chemist who had been asked several times, when there were three items on prescriptions, which one was important because the mother could not afford the other two till the end of the week. Mr. POWELL explained that there were many factors which no doubt played a part in the fall between February and March, and which made the March figure in itself of little help and guidance—for example, the influenza epidemic ended before the end of February, and this year March was exceptionally fine. Mr. K. ROBINSON said the Minister had estimated a 2% fall in prescriptions but had got a 20% drop. This compared also with increases in February and March last year. Was not this evidence that people were not getting the prescriptions they needed? Mr. POWELL said it was not. They could not take individual months without regard to the circumstances. No less than experience over the whole year could disclose any trends which were capable of being interpreted in that way.

Sir HUGH LINSTEAD (Putney, Con.) suggested that it might be wise for the Minister to initiate an inquiry to find out what the situation was, in view of the differing evidence and opinions. Mr. POWELL answered that he still thought it was too early for anything of that kind. He was sure that the professions and bodies that administered the Service would bring to his attention any evidence that came their way.

Hammersmith Hospital Secretary

Mrs. JOYCE BUTLER (Wood Green, Lab.) asked the Minister on June 2 if he had reached a decision with regard to an inquiry into the appointment of a new secretary to the board of governors of the Hammersmith Postgraduate Teaching Hospital. Mr. POWELL said yes. Having obtained a full statement from the board of governors on the circumstances surrounding this appointment, he had come to the conclusion that they disclosed no reason for an inquiry. He had so informed the Institute of Hospital Administrators, who had asked him to set up an inquiry, and had sent them a copy of the statement.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The Sir Lionel Whitby Medal for 1959–60 has been awarded to Dr. C. W. M. Adams.

In Congregation on May 13 the degree of M.B. was conferred on J. D. Geddes.

UNIVERSITY OF ABERDEEN

Mr. C. G. Clark has been appointed to a senior lectureship in surgery from July 12, 1961.

The following have been appointed to terminable Lectureships in Anatomy during the periods indicated in parentheses: Dr. G. S. Robertson and Dr. Manik Singh (April 1 to September 30, 1961); Dr. W. L. Armstrong and Dr. R. L. Gordon (October 1, 1961, to September 30, 1962); and Dr. W. R. C. Turner and Dr. A. I. G. Davidson (September 1, 1961, to August 31, 1962).

Dr. G. M. M. Robb has been appointed to a terminable Lectureship in Biological Chemistry from October 1, 1961, to September 30, 1962.

UNIVERSITY OF LONDON

On Foundation Day, November 23, the honorary degree of D.Sc. will be conferred on Sir Howard Florey, F.R.S., and the honorary degree of LL.D. on Sir Francis Fraser.

Dr. O. J. Lewis, Senior Lecturer at St. Bartholomew's Hospital Medical College, has been appointed to the University Readership in Anatomy tenable at that College.

The title of Professor of Urology in the University has been conferred on Mr. Ralph Shackman in respect of his post at the Postgraduate Medical School of London.

The following candidates have been approved at the examinations indicated:

THIRD M.B., B.S.—[1] [6]Anne C. Berry, [1] [3]L. M. Blendis, [1] [6]A. J. Bonn, [1] [3]T. J. H. Clark, [1] [2]M. H. Devereux, [1] [3]R. M. B. Dowling, [1] [5]D. Faro, [1] [6]Audrey J. E. Flower, [1] [5]J. Gerwat, [1] [4]G. J. T. Lewis, [1] [5]Ann-Mary E. Macdonald, [1] [3]C. S. Ogg, [1] [4]Ilfra J. Pink, [1] [5]D. S. Reeves, [1] [2] [4] [6]Linda M. Skolar (University Medal), [1] [5]G. H. Smith, [1] [5]G. P. Williams, [1] [5]F. J. Woodroffe, M F. A'Brook, Katherine J. Adcock, M. Aidoo, S. Al-Khedheri, Betty J. Allen, C. D. Allen, R. T. J. Allen, Kathleen M. Allsopp, E. J. J. Almeida, K. Ametewee, A. C. Antcliff, P. P. Anthony, Ann P. Appleby, R. F. Armstrong, Roma S. Ashby, Lesley B. Ashworth, D. A. Aubrey, J. C. C. Ayling, H. Baddeley, Rosemarie A. Baillod, B. L. Baker, J. S. Ball, J. L. K. Bankes, Alexandra L. H. Barber, E. Barker, G. Barlow, Judith A. Barnard, Bernice M. S. Barnett, J. J. D. Bartlett, T. P. Bartlett, C. G. Beardwell, H. B. Begg, M. S. Bell, A. R. Bellau, C. L. Berry, D. B. Berzoa, A. C. Bird, C. G. Bird, M. B. J. Bishop, M. Black, Sheena Blackburn, Frances M. Blydenstein, Anne J. V. Boardman, C. J. Bolt, R. A. Bond, Mavis A. Bonnard, C. A. Booth, H. C. Booth, J. C. Bouch, J. M. H. Boyce, Lorna W. Bratton, P. J. Brewer, H. W. E. Briscoe, A. J. Bron, E. J. Brown, J. Brown, Lorna A. Brown, R. N. Brownfield, D. A. Bryan, W. Bunting, C. R. Campin, R. A. N. Caplan, J. W. Carswell, E. J. P. P. F. Caruana-Galizia, Shirley G Castle, M. E. Cavendish, Heather C Chapman, Margaret W. Childe, I. N. Chima, K. F. Chittenden, John Chung Kwai Choy, P. J. Clarkson, N. G. Cockman, S. L. Cohen, Christine M. Colley, J. M. Collis, Jane E. Colliss, N. B. E. Cooter, Penelope A. Cove-Smith, D. R. Covington, W. S. C. Cox, D. R. Dadge, D. G. Daniel, Judith M. Darmady, Gillian Davey, D. LI. Davies, J. D. Davies, M. J. Davies, R. P. Davies, D. M. Denison, S. B. R. Desai, H. M. A. Dixit, Margaret J. Dixon, R. Dixon, R. J. Donnelly, J. A. Dormandy, P. J. Doust, F. P. T. Drake, R. M. Drake, A. M. Driscoll, Maureen B. Duggan, Joy B. Edelman, R. S. Edmondson, D. F. Elson, C. W. Elston, D. A. Evans, C. V. Everard, P. R. H. Evison, R. W. T. Farley, M. J. Farr, Barbara V. Faulk, T. Feizi, R. H. Fell, T. J. ffytche, I. T. Field, C. J. Fielding, Shirley M. Fisher, J. M. T. Ford, R. France, S. Gallannaugh, R. H. Gandy, S. W. Garland, A. F. Gazdar, Vera Gellert, M. A. N. Ghods, B. V. Gill, H. M. Gillespie, L. J. Goldfine, Kathleen M. Goodwin, D. N. Gordon, Rosamund Gould, Sally M. Grantham, Judith Greenwood, B. W. Griffiths, D. J. Grundy, D. G. Gwyn, J. D. Hailstone, Jennifer M. Hall, J. H. Hall, M. S. Hall, J. F. Hallpike, R. E. Hamill, Ruth Hamilton, J. A. Hanne, I. W. Hanwell, J. C. Harding, M W. Harper, N. P. A. L. Harper, D. L. Harris, Deirdre A. Hart, J. C. D. Hart, I. C. Harvey, D. J. Hatch, W. E. Hawes, Judith M. Hawker, T. J. Hawkins P. M. Hayward, S. Hazboun, D. C. Herbert, E. B. Herd, Penelope B. Hewitt, Doreen M. Heyworth, B. M. Hogbin, Tessa Holman, J. T. Holmes, Hilary J. Honey, J. Hood, A. P. Hopkins, Alisa Hornung, Barbara J. Horrell, P. M. B. Howard, Margaret E. Hughes, Kathleen M. Hunt, W. J. Hunter, L. A. Hurt, D. W. Hyatt, M. Indech, Angela M. H. Jackson, Marianne Janosi, M. I. V. Jayson, Anne M. Jéquier, D. L. Johns, M. G. Johnson, P. M. Johnson, B. M. Jones, T. Kajtar, P. G. Kay, Susan Kay, Anne B. Kenshole, Heather S. Kerr, Penelope J. Key, D. E. L. King, M. H. King, N. J. W. Kippax, Veronica Kirton, Coral R. Knight, E. K. Korley, Heather Lachlan, W. A. Landers, Eileen Larkin, R. G. C. Lett, Cynthia N. A. Levett, W. A. Lindsay, A. J. Lines, Jennifer Lloyd, Barbara V. Longley, T. J. McCarthy, Mary B. MacKeith, Jean McKinnon, Fatemeh E. Mahjd, A. C. J. Maendl, Micheline M. Maher, J. K. C. Maile, D. E. I. Mais, Cynthia M. Marcon, R. H. Marston, D. J. Martin, J. P. Martin, M. H. J. Martin, C. A. S. Mason, D. Mathias, B. F. Meggitt, Lucy Mensah, D. S. Miller, Helen R. Miller, M. Millington, Diana E. Millward, Mary C. Milne, Patricia J. Money, Maldwyn Morgan, Ruth M. Morris, P. R. Mortimer, D. B. Moss, Julia A. Munro, M. Murray, Judith C. Naylor, Pauline M. Naylor, J. M. Nocton, P. M. J. O'Donnell, P. M. O'Driscoll, J. A. Ogyaadu, N. J. Osborn, B. W. Otridge, A. Padfield, M. E. Paul, R. H. Pearce, Margaret Pedlar, R. A. Peebles, M. C. O. Phillips, M. C. Pietroni, Margaret N. R. Pitt, Dorothy E. Platts, J. O. M. Pobee, A. J. Poole, Bernadette M. V. Porter, E. W. Powell, G. A. Prall, A. Prestwich, M. G. Prinn, W. G. Prout, W. E. M. Pryse-Phillips, B. W. Pullen, Margaret Pyke, D. C. Quantock, M. C. Rallings, R. G. Rathbone, Kathleen F. Rayner, A. J. Reed, C. P. Reynolds, Janis M. Richmond, D. M. Ricks, Joyce M. Robinson, Valerie A. Rogers, Joy G. Roworth, Jane D. D. Rowswell, Bridget A. Rylands, K. Safo-Adu, S. Sahai, J. B. Sales, R. W. Salmon, A. H. Sarafian, S. H. Saunders, R. J. Schick, A. Schulman, D. Shaffer, A. B. Shaw, Brenda N. Shaw, A. C. F. Sjögren, Vivienne A. Skinner, M. A. Skivington D. H. Smith, H. D. Smith, Jacqueline Q. Smith, P. N. Sperryn, T. A. Spratley, T. N. Stanbridge, S. L. R. Stanton, D. Steel, D. L. Stevens, R. Stilwell, N. Stoddart, E. Stonehill, J. C. H. Strachan, Margaret E. Tambiyn, Angela C. Telfer, A. C. Templeton, G. M. Theobald, L. K. H. Therkildsen, G. O. Thomas, Valerie J. Thomas, W. H. F. Thomson, A. E. Thorn, J. G. B. Thurston, K. A. Turner, Sophie S. Turner, Elizabeth J. Tytler, Rosemary A. Underhill, J. M. Varney, J. P. Vaughan, Frances Wahl, Pamela G. Wales, B. A. Wallace, B. B. Wallace, Sheila L. Waller, Barbara C. Walsh, E. R. Walrond, J. B. Watkins, B. M. Watson, M. Watson, L. M. Webber, A. D. Wedderspoon, Sally K. Weeks, D. J. Westlake, T. K. Wheeler, D. C. Whyte, D. H. Wickenden, B. T. Williams, Margaret Williams, C. E. R. Winer, B. E. P. Wookey, B. J. Woolford, R. J. Worden, Ann F. Worsfold, Adela W. Wright, I. G. Wylie, Caroline R. S. M. Wynne-Roberts, E. Young, M. A. Zatouroff.

[1]With honours. [2]Distinguished in pathology. [3]Distinguished in medicine. [4]Distinguished in applied pharmacology and therapeutics. [5]Distinguished in surgery. [6]Distinguished in obstetrics and gynaecology.

UNIVERSITY OF BIRMINGHAM

The following representatives have been appointed: Professor A. L. d'Abreu, Professor W. Melville Arnott, Professor T. McKeown, and Dr. A. G. W. Whitfield, on the Standing Joint Committee of the University, the United Birmingham Hospitals, and the Birmingham Regional Hospital Board for the year April 1, 1961, to March 31, 1962; and Dr. T. L. Hardy on the Worcestershire Local Medical Trainee Practitioner Scheme.

Sir Francis Knowles, Lecturer in Anatomy, and Dr. E. C. Fox, Lecturer in Dental Surgery, have been promoted to Senior Lectureships from October 1, 1961.

The title of University Research Fellow has been conferred on Dr. G. M. Aber, Senior Registrar attached to the Medical Professorial Unit, for the tenure of his present appointment, or for the period of his stay at the University.

UNIVERSITY OF LIVERPOOL

Dr. Harold Wilson has been appointed Senior Lecturer in Pharmacology from October 1, 1961.

UNIVERSITY OF SHEFFIELD

The following appointments are announced:—*Full-time:* Dr. J. M. Hudson, Dr. G. J. Lloyd, and Dr. B. K. Sood, Demonstrators in Anatomy; and Dr. V. Dubowitz, Lecturer in Child Health. *Part-time:* Dr. A. C. Woodmansey, Clinical Teacher in Psychiatry; Mr. J. T. Rowling, Clinical Teacher in Surgery; and Dr. A. Stanworth, Lecturer in Ophthalmology.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on May 11, with Sir Arthur Porritt, President, in the chair, a resolution of condolence was passed on the death of Professor Julian Taylor, a member of Council.

Dr. E. Rohan Williams (St. Mary's Hospital) was admitted as a Fellow by election, and Mr. T. A. Ogilvie, F.R.C.S.Ed., was elected to the Fellowship *ad eundem*.

A certificate of honourable mention for the Jacksonian Prize for 1960 was presented to Mr. H. Hamilton Stewart, of Bradford.

The Cartwright Prize for 1960 was presented to Professor G. L. Howe, of Newcastle upon Tyne. A certificate of honourable mention for the Cartwright Prize for 1960 was presented to Mr. H. P. Cook, of the Middlesex Hospital.

The Begley Prizes were awarded to Miss Susan Key, of the University of Liverpool, and Miss Rosemary Raymonde Norton, of Guy's Hospital Medical School.

The President was appointed as representative on the governing body of the British Postgraduate Medical Federation for the year 1961–2.

Mr. A. Hedley Whyte was reappointed as representative on the council of King's College, Newcastle upon Tyne.

The Laming Evans senior research fellowship of Mr. R. G. Smith was renewed for a second year from April 19, 1961.

A Diploma in Anaesthetics was granted, jointly with the Royal College of Physicians of London, to J. M. Cundy.

After the meeting the first Bland-Sutton Lecture was delivered by Dr. Frank Stansfield on "Sir John Bland-Sutton, 1855–1936: His Life, Habits, and Friends."

Vital Statistics

Road Casualties in March

There were 581 deaths from road accidents during March. Of this total 252 were pedestrians, 46 were pedal-cyclists, 127 were motor-cyclists, scooter, or moped riders, and 156 were drivers and passengers in cars and other vehicles. In addition, 6,317 persons were seriously injured. The March figures brought the death roll on the roads during the first three months of 1961 up to 1,548, an increase of 90, or over 6%, compared with the corresponding months of 1960. Motor traffic is estimated to have increased by about 12% over the same period.

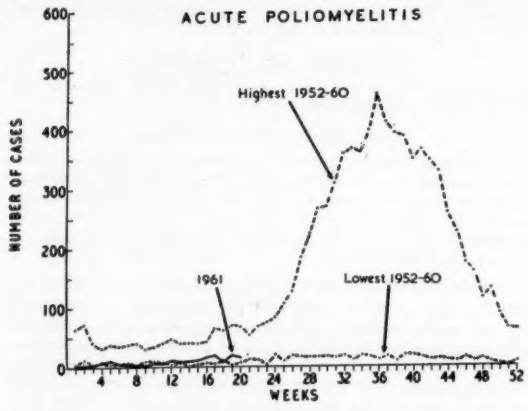
Infectious Diseases

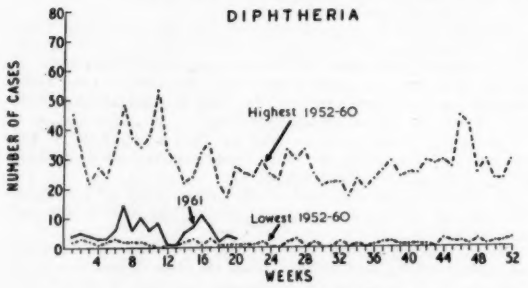
Although the epidemic of *measles* is subsiding, the notifications during the week ending May 27 were still running at a high level, particularly in Bristol, Stoke-on-Trent, Croydon, Brighton, Birmingham, and Leeds. In Birmingham also seven cases of *acute poliomyelitis* were notified. In an outbreak of *food-poisoning* in Gosport 114 cases were notified.

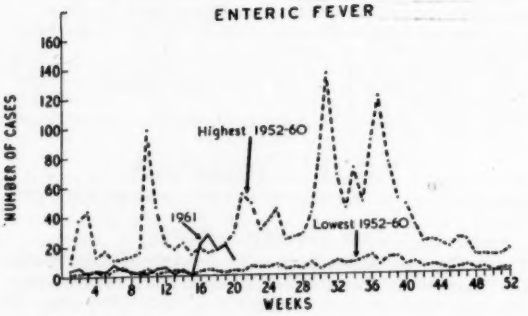
Graphs of Infectious Diseases

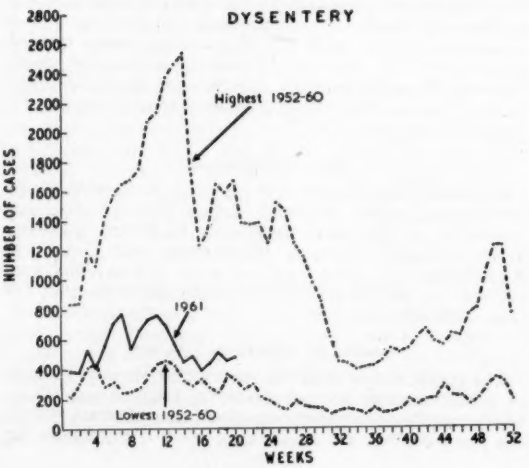
The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for

1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 20** (No. 20) and corresponding week 1950.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	3	1	0	4	2	0	3	0	
Dysentery	479	57	110	1	14	1,151	141	200	8	11
Encephalitis, acute	2	0		0		4	0	1	1	
Enteric fever:										
Typhoid	1	0	0	0		1	1	0	0	
Paratyphoid	10	3	1 (B)	0		12	0	0	0	
Food-poisoning	169	19	33	0		151	29	5	0	
Infective enteritis or diarrhoea under 2 years				14	55				22	18
Measles*	24,320	873	345	349	220	1,883	88	39	6	21
Meningococcal infection	12	3	7	0		20	2	5	1	1
Ophthalmia neonatorum	26	2	3	0		21	1	2	0	
Pneumonia†	223	16	159	5		250	14	163	3	
Poliomyelitis, acute:										
Paralytic	11	1	0	1		2	0	0	0	5
Non-paralytic	3	1	0			5	2	0		
Puerperal fever§	141	23	9	2		209	40	8	1	
Scarlet fever	448	32	28	18	6	620	30	53	20	20
Tuberculosis:										
Respiratory	390	48	70	18		464	60	73	29	
Non-respiratory	66	2	17	5		67	6	4	3	
Whooping-cough	524	15	34	5	45	1,458	108	225	3	76

DEATHS	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	12	0	0	1	3	4	0	0	0	0
Influenza	7	1	0	0	0	13	1	5	1	0
Measles		0	1	0	1		0	0	0	0
Meningococcal infection		0	0				0	1		
Pneumonia	417	38	19	19	3	458	33	21	21	5
Poliomyelitis, acute	1	0		0	0	1	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	54	3	3	1	1	49	6	2	6	
Non-respiratory		0		0	0		2	1	0	
Whooping-cough	0	0	0	0	1	1	0	0	0	0
Deaths 0–1 year	307	35	33	14	17	329	34	17	6	7
Deaths (excluding stillbirths)	9,522	783	585	117	155	9,227	734	587	138	142
LIVE BIRTHS	16,427	1358	1065	301	463	16,080	1253	1023	284	463
STILLBIRTHS	279	20	25			341	19	29		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Film Competition, 1961

To encourage the production of good medical films the Council of the B.M.A. offers medals and certificates for 16-mm. medical films to be submitted in open competition. Awards will be considered in two categories—for commercial and non-commercial film producers. Only films completed within the two years before September 30 may be entered for the competition. Details and entry forms may be obtained from the Secretary, B.M.A. House, Tavistock Square, London W.C.1. The closing date for receipt of entry forms is September 30, and for films November 15.

New Head of Division of Bacteriology and Virus Research, Mill Hill

Dr. ALICK ISAACS succeeded Sir CHRISTOPHER ANDREWES, F.R.S., as head of the division of bacteriology and virus research at the National Institute for Medical Research, Mill Hill, on June 7.

Dr. Isaacs qualified M.B., Ch.B. at Glasgow University in 1944, and subsequently spent two years at the Walter and Eliza Hall Institute of Medical Research in Melbourne as a Rockefeller Travelling Research Fellow. When he returned to Great Britain in 1950 he joined the National Institute at Mill Hill, where he is currently carrying out research on interferon. Dr. Isaacs gained his M.D.(Glasgow) in 1955 with Gold Medal.

Dr. H. G. PEREIRA took charge of the W.H.O. World Influenza Centre at the National Institute from the same date.

Chair of Oral Medicine, Welsh National School of Medicine

Dr. B. E. D. COOKE, reader in dental medicine at Guy's Hospital Dental School, has been appointed to the chair of oral medicine and as dean of dental studies at the Welsh National School of Medicine. He will take up his appointment on August 1 next year in preparation for the new dental school and hospital which is to be built in Cardiff.

Dr. Cooke, who was born in 1920, was educated at Merchant Taylors' School, and at the London Hospital Medical and Dental Schools, where he qualified L.D.S. R.C.S.(Eng.) in 1942 and M.R.C.S. (Eng.) and L.R.C.P.(Lond.) in 1949. From 1943 to 1946 he served as dental surgeon in the Royal Naval Volunteer Reserve. From 1949 to 1950 he was senior dental registrar at the London Hospital Dental School, and from 1950 to 1951 was Nuffield Fellow in General Pathology in the Bernard Baron Institute of Pathology at the London Hospital. He went to Guy's Hospital in 1951 as Nuffield Fellow in Oral Pathology in the department of dental medicine, becoming senior lecturer there in 1953 and reader in dental medicine in the same department in 1958. He was awarded the Cartwright Prize and Medal of the Royal College of Surgeons of England for the years 1950 to 1955, and the Chesterfield Prize and Medal awarded by the Postgraduate Institute of Dermatology, St. John's Hospital for Diseases of the Skin, London, for the year 1955. He has written a number of papers on various aspects of dental medicine and oral pathology, and is joint author of *Oral Histopathology*.

Chair in Medical Statistics, Queen's University, Belfast

Dr. E. A. CHEESEMAN, B.Sc.(Econ.), Ph.D., has been appointed to the chair in medical statistics in the department of social and preventive medicine at the Queen's University of Belfast.

New Bristol Chair of Mental Health

A new chair of mental health is to be established in the University of Bristol. A professor will be chosen shortly to head a department of mental health which will absorb the University's existing department of psychiatry. He will have special facilities for research into preventable mental illness. This new chair will be endowed by donations from the Van Neste Foundation and from the late Mrs. N. COOKE-HURLE. Mrs. Cooke-Hurle was an honorary graduate and had been a member of the University council since 1909.

Faculty of History of Medicine and Pharmacy

The Honorary Fellowship of the Faculty of the History of Medicine and Pharmacy was awarded to Sir ARTHUR MACNALTY and Sir ZACHARY COPE in recognition of their long and distinguished services to the history of medicine at the Faculty's annual general meeting at Apothecaries' Hall. The meeting was told that the membership of the Faculty, after only two years' existence, already stood at 304, and that 65 universities, medical schools, and postgraduate institutes had enrolled as Corporate Members. On the initiative of the Faculty, St. Thomas's Hospital Medical School had appointed a "Society of Apothecaries Lecturer in the History of Medicine," and the governing body of King's College Hospital Medical School had approved the establishment of a similar appointment there. The Faculty's endowed lectures had now been named: the Annual Students' Lecture would henceforth be known as "The Osler Lecture," and the Autumn Lecture would be named "The Sydenham Lecture."

American Monograph Prizes

The American Academy of Arts and Sciences is awarding three prizes of $1,000 each "to the authors of especially meritorious unpublished monographs, one each in the fields of the humanities, the social sciences, the physical and biological sciences." Details may be obtained from the Committee on Monograph Prizes, American Academy of Arts and Sciences, Little Hall 33, Harvard University, Cambridge 38, Massachusetts, U.S.A. The closing date is October 2.

Grants, Gifts, and Bequests

A grant of £78,125 has been made under the Colonial Development and Welfare Act for a new preclinical building at the University of Hong Kong.

People in the News

Dr. J. L. BLONSTEIN has been awarded the gold medal of the Amateur Boxing Association for long service.

Sir ARTHUR MASSEY, chairman of the council of the Royal Society of Health, and formerly Chief Medical Officer of the Ministry of Pensions and National Insurance, has been appointed a trustee of the Chadwick Trust in place of Lord AMULREE, who has resigned.

Dr. J. K. WALES has been awarded the first annual Maccabaean Prize (25 guineas) and Medal of the Faculty of the History of Medicine and Pharmacy for his essay on "The Historical Relations between Chemistry and Medicine." At the time of his entry he was a final-year medical student at the University of Leeds.

Dr. R. B. BUZZARD, of the Medical Research Council's Industrial Psychology Research Unit, has been appointed research director of the National Institute of Industrial Psychology.

Dr. WILLIAM BUCHANAN, of Pollakshields, Glasgow, has been awarded an international post-doctorate research fellowship by the National Institutes of Health, United States Public Health Service. He will study autoimmunity at the U.S. National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland.

Dr. H. JACKSON, head of the department of experimental chemotherapy, Christie Hospital, Manchester, has been

awarded the Family Planning Association's 1960 Oliver Bird Prize for his paper, "Anti-fertility Substances and their Assessment in the Male Rodent."

Mr. SOMERSET MAUGHAM has become the first Englishman to be made an honorary Senator of Heidelberg University. The award was conferred during a ceremony to mark the 575th anniversary of Germany's oldest university.

Professor RALSTON PATERSON has been awarded the Gold Medal in Therapeutics of the Society of Apothecaries of London "in recognition of his outstanding work in the field of radiotherapy." It will be presented on June 20.

COMING EVENTS

Ernestine Henry Lecture.—Dr. J. M. BARNES, "The Mode of Action of Some Toxic Substances with Special Reference to the Effects of Prolonged Exposure," June 20, 5 p.m. See advertisement p. 57.

Indian Medical Service.—Dinner, June 23, East India and Sports Club, St. James's Square, London S.W.1. Applications to Dr. P. H. ADDISON, 27 Sudbury Court Drive, Harrow.

Oxford Graduates Medical Club.—Summer dinner, June 24, Pembroke College, Oxford. Chairman: Mr. T. HOLMES SELLORS. Details from Dr. R. BRYCE-SMITH, Department of Anaesthetics, Radcliffe Infirmary, Oxford.

National Association for Mental Health.—Meeting arranged in collaboration with Churches' Council of Healing and Central Churches Group of the National Council of Social Service, "The Work of the Academy of Religion and Mental Health in the U.S.A. and Relevant British Experience," June 26, 3 p.m., Barnes Hall, Royal Society of Medicine, 1 Wimpole Street, London W.1. Details from N.A.M.H., 39 Queen Anne Street, London W.1.

Tuberculosis Society of Scotland and British Tuberculosis Association.—Annual conference, Edinburgh, June 29–July 1. Details from, and applications to, by June 24, Administrative Secretary, B.T.A., 59 Portland Place, London W.1.

Cambridge Graduates' Medical Club.—Annual general meeting and dinner, June 30, Sidney Sussex College. Members who have not received notice, and any others interested, write to Mr. H. H. E. BATTEN, 67 Bridge Street, Cambridge.

Nutrition Society. — Symposium, "Nutrition and Metabolic Defects," July 15, 11 a.m., Laboratory of Physiology, Oxford. Chairman, Sir HANS KREBS, F.R.S. Details from Miss D. F. HOLLINGSWORTH, c/o Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, London S.W.1.

Whittington Hospital.—Symposium, "Chest Diseases in Children," July 26, 11.30 a.m., Whittington Hospital, Museum Lecture Theatre, Archway Wing, Archway Road, London N.19. Details from Dr. P. D. B. DAVIES, St. Pancras Chest Clinic, 26 Margaret Street, London W.1.

Henry Head Centenary Celebrations.—Meeting to celebrate centenary of Sir Henry Head's birth, August 31, 3 p.m., New Students' Hall, The London Hospital, London E.1. Speakers: Sir RUSSELL BRAIN, Dr. MACDONALD CRITCHLEY, Professor K. W. CROSS, Dr. R. A. HENSON. Those who wish to attend should notify Dr. R. A. HENSON at the above address by August 17.

2nd Middle Eastern-Mediterranean Paediatric Congress.—Ankara, September 6–9. Details from Hacettepe Cocuk Hastahanesi, Ankara, Turkey.

2nd International Conference of Human Genetics.—Rome, September 7–12. Details from Secretariat, Istituto Gregorio Mendel, 5 Piazza Galeno, Rome, Italy.

5th International Congress of Electroencephalography.—Rome, September 7–13. Details from Secretary-General, Dr. RAFFAELLO VIZIOLI, 30 Viale Università, Rome, Italy.

7th International Congress of Neurology.—Rome, September 10–15, under auspices of World Neurologic Federation and National Institute for Nervous Diseases and Blindness, of Bethesda, U.S.A. Details from the Secretary-General, Dr. GIOVANNI ALEMÀ, 30 Viale Università, Rome.

University of London Postgraduate Medical School.—Advanced symposium for consultants, "Modern Aspects of Cardiovascular Radiology," September 21–23. (See advertisement, p. 57.)

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, June 10

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Benenden Chest Hospital, 10.30 for 11 a.m., Dr. A. L. R. Mayer, Dr. E. Williams, and Dr. M. Houri: Assessment and Treatment of Chronic Bronchitis.

Monday, June 12

INSTITUTE OF DERMATOLOGY.—At British Institute of Radiology, 5 p.m., Mr. R. E. Ellis: Radiation Hazards and Protection (I).

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Brian Ackner: Stress and Psychosomatic Illness.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: METROPOLITAN BRANCH.—At Lecture Theatre, London School of Hygiene and Tropical Medicine, 2.30 p.m., Dr. Henry Kempe (WHO): Smallpox.

Tuesday, June 13

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute, 5 p.m., Dr. Desmond O'Neill: Gynaecological Neuroses.

Wednesday, June 14

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Interesting Histological Sections.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. T. Holmes Sellors: Problems in the Treatment of Fallot's Tetralogy.

LEWISHAM GENERAL HOSPITAL.—5.45 p.m., Dr. A. R. Norton: Chemotherapy of the Psychoses.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. Honor B. Fell: Tissue Culture in Experimental Pathology.

ROYAL FREE HOSPITAL, Gray's Inn Road, London W.C.—5.15 p.m., Dr. Selwyn Baker (Vellore): Sprue.

Thursday, June 15

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26 Portland Place, London W., 7.30 p.m., annual general meeting; 8 p.m., Professor P. C. C Garnham: Vector of *Hepatocytis* (=*Plasmodium kochi*): The Successful Conclusion of Observations in Many Parts of Tropical Africa.

LONDON UNIVERSITY.—At King's College, Strand, W.C., 5.30 p.m., special university lecture in pharmacology by Professor L. Goldberg (Stockholm): Alcohol and Addiction.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. J. Hamilton Paterson: postgraduate demonstration in neurology.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: SOUTHERN BRANCH.—At Salisbury Council Chamber, 3 p.m., Dr. J. F. Skone: Health of the Immigrant.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Zoological Gardens Restaurant, annual banquet.

Friday, June 16

BRITISH INSTITUTE OF RADIOLOGY.—At Reid-Knox Hall, 32 Welbeck Street, London W., 2.15 p.m., Radiobiology Meeting. Short papers will be read.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. N. W. Roberts: Osteochondritis Dissecans.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Welch.—On May 29, 1961, to Margaret Louise (formerly Fisher), M.B., Ch.B., B.A.O., and Gordon Welch, M.D., M.R.C.P., of West Hartlepool, Co. Durham, a brother for Gillian.

DEATHS

Alexander.—On May 20, 1961, John Budge Alexander, M.D., D.P.H., of Altrumas, Weem, Aberfeldy, Perthshire, aged 79.

Denny.—On May 19, 1961, at a London hospital, Cedric Roland Denny, M.R.C.S., L.R.C.P., aged 68.

Donald.—On May 23, 1961, at a hospital, Glasgow, John Donald, M.B., Ch.B., of 6 Victoria Road, Gourock, Renfrewshire.

Fawkner-Corbett.—On May 19, 1961, at 34 Cumberland Court, Southsea, Hants, William Victor Fawkner-Corbett, M.R.C.S., L.R.C.P., D.P.H., Lieutenant-Colonel, R.A.M.C., retired.

Gordon.—On May 15, 1961, at 42 Wetherby Road, Leeds, Yorks, Valentine Henry Gordon, M.B., Ch.B., late of York, Western Australia, Exeter, and Guernsey, aged 80.

Hamilton.—On May 23, 1961, at Alderney, Edgar Alan Hamilton-Pearson, M.B., Ch.B.

Keyworth.—On May 12, 1961, in a nursing-home, near Winchester, Hants, William David Keyworth, M.D., M.R.C.P., Lieutenant-Colonel, I.M.S., retired, of St. Mary Bourne, near Andover, Hants, aged 80.

Macmillan.—On May 22, 1961, at a nursing-home, Bexhill, Sussex, Charles Clarke Macmillan, D.S.O., M.B., C.M., Surgeon Commander, R.N., retired, formerly of Hamilton, Australia, aged 88.

Nicholson.—On May 16, 1961, in hospital, Dublin, Margaret Nicholson, M.B., B.S., late of Castlemount, Castleknock, Co. Dublin.

Pulteney.—On May 11, 1961, in London, Isabel Pulteney, M.D., aged 94.

Selby.—On May 16, 1961, at home, 52 Castlebar Road, Ealing, London W., Edward James Selby, O.B.E., M.R.C.S., L.R.C.P.

Taylor.—On May 14, 1961, George Orissa Taylor, M.B., of Reigate, Surrey, Islington and Nilgiri Medical Missions, aged 87.

Young.—On May 14, 1961, at Moffatt House Hotel, Dumfriesshire, Hugh Young, M.B., Ch.B., of Aigburth, Liverpool.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Chronic Q Fever

Q.—*What is the treatment for persisting pyrexial episodes after an attack of Q fever? In the initial attack there was a positive titre for Q fever of 1/80. One month later it was 1/640, and four months after that 1/320. Five-day courses of tetracycline initially and recently were of no lasting benefit.*

A.—Although the majority of patients with Q fever respond to treatment with tetracyclines, it is recognized that some otherwise uncomplicated cases fail to do so.[1] Also a minority of patients have one or two febrile relapses after the acute illness. Chloramphenicol (full dosage, depending on the age and weight of the patient) may be tried as an alternative treatment and its use continued for a few days after the febrile relapse subsides.

If these febrile episodes continue to occur despite an attempt at treatment with chloramphenicol, then the patient should be thoroughly investigated to exclude (*a*) chronic Q fever, and (*b*) any coexisting or other infections—e.g., brucellosis. Chronic Q fever has been shown to occur as a subacute rickettsial endocarditis affecting the heart valves,[2 3] and there is also a theoretical but unproved possibility that a chronic infection might be superimposed on some diseased organ other than the heart. Serological examination for the rare Q fever Phase 1 complement-fixing antibody may provide a valuable pointer to the existence of a chronic Q fever state, and attempts to isolate the rickettsia from the blood during a relapse may also be indicated. These specialized tests can be arranged through the local laboratory of the Public Health Laboratory Service, which should be consulted.

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Acute Diabetic Abdomen

Q.—*Attention was recently called[1] to the importance of the acute diabetic abdomen. What is the mechanism of its occurrence, and how can it be differentiated from an acute surgical condition?*

A.—The mechanism of the acute diabetic abdomen is improperly understood, but most authorities[2 3 4] consider it to be due to muscular cramps occurring in the accessory respiratory muscles of the lower thorax and upper abdomen produced by changes in the plasma electrolytes as a result of the ketosis. Both the sodium and potassium are reduced, and naturally any muscular cramps caused thereby will occur in those muscles which are being actively used—in this case, the accessory respiratory muscles. However, this may not be the true explanation, and the matter is imperfectly understood. It may be differentiated from an acute surgical abdominal emergency by a number of factors which must be assessed jointly. First, diabetes obviously must be present, together with ketosis. Secondly, in the acute surgical abdomen the vomiting is almost always preceded by abdominal pain, whereas in the acute diabetic abdomen the vomiting precedes the abdominal pain. Thirdly, effective and vigorous treatment of the ketosis with insulin and saline infusions will cause the pain to disappear rapidly in three or four hours without the use of any analgesic drugs. It must, of course, always be borne in mind that an acute surgical emergency may occur in a diabetic patient. In such cases, if there has been no improvement after the above treatment has been pursued for a few hours, the abdomen should be opened, if possible under local anaesthesia. Another pointer is that in the acute surgical abdomen muscular guarding or rigidity is likely to be a more prominent feature than in the diabetic abdomen. This matter is referred to by Howard F. Roote.[5]

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Incidence of Appendicitis

Q.—*There appears to have been a marked decrease in the incidence of acute appendicitis in my practice in the past few years. Is this so generally, and, if so, what might be the reason? Could the widespread use of antibiotics for various infections have tended to resolve latent foci of appendicular infection?*

A.—To the writer's knowledge there is no information from widespread sources to show that there has been a national decrease in the incidence of acute appendicitis. There are, however, some indications that not all cases diagnosed as acute appendicitis are regarded as being quite so urgently in need of surgical treatment as was once advocated. This means that there is time for further consideration which may lead to a change of diagnosis.

Every conscientious surgeon will acknowledge that he has at times removed appendices in cases where the sole confirmation of the diagnosis rested upon the pathologist's report that "inflammatory changes are seen." Then again there is the increasing realization that cases of appendicular inflammation may sometimes be manifestations of a generalized affection of lymphoid tissues which will respond to treatment of the general condition, often by antibiotics; to that extent the answer to the question is in the affirmative.

Nevertheless, it would be interesting to know whether there has been a true decrease in the incidence of proved cases of acute appendicitis, since this might afford a clue to its aetiology. Up to the present the many papers and books on the subject have propounded as many different views of the causative factors.

Chronic Cervicitis

Q.—*Some years ago chronic cervicitis was commonly regarded as a cause of backache, abdominal pain, and general ill-health. Is it still so regarded, and does treatment relieve the symptoms?*

A.—Chronic cervicitis, like chronic endometritis, is disappearing from the vocabulary of the critical gynaecologist and pathologist. If by the term is meant the end results of trauma and of past infection, the diagnosis can be made in almost all multiparous women. The changes can be seen microscopically if not macroscopically. But they cannot be regarded as significant unless concomitant glandular overactivity, also a result of previous irritation, causes a profuse mucoid discharge. Even then, and while admitting that opinion varies, I do not consider that this condition causes backache, abdominal pain, and general ill-health unless it is complicated by clear signs of associated "chronic cellulitis" in the broad and utero-sacral ligaments. This again is quite exceptional, and its physical signs really represent nothing more than post-inflammatory fibrosis.

When alleged chronic cervicitis is treated by diathermy coagulation or by surgery in the belief that it is causing general symptoms of the type mentioned, the patient often obtains relief, at least for a time. This, however, is not explained by the elimination of "chronic cervicitis." The

effect may in part be psychological, but is mainly because the need to have an operation and to enter hospital brings to a harassed woman her only opportunity to rest her aching muscles, to be relieved of her daily household responsibilities, and to receive the sympathy and attention of relatives and friends which she would otherwise not obtain. To have her cervix cauterized is sometimes a tired housewife's only means of prompting her husband to give her a bunch of flowers, to bring her tea to bed in the morning, and to help with the washing up.

Gelatin for Brittle Nails

Q.—*Advertisers recommend taking gelatin for various beauty purposes, the suggestion being that it is a "remedy for brittle and breaking finger-nails." Is there any evidence to support such a claim?*

A.—I am not aware of any convincing evidence to support this claim. Gelatin has been recommended as a treatment for psoriasis of the nails. From my own experience I believe that it is sometimes, though by no means always, effective. When it is, a daily dose of about ½ oz. (14.2 g.) of gelatin has to be taken for a period of usually at least two or three months before improvement is evident. If the treatment is stopped the psoriasis of the nails is likely to relapse in the course of a similar period of time. Fragile and brittle nails[1] are not usually the result of psoriasis, and I doubt whether gelatin treatment will affect this complaint. In any event, one would hardly expect to see improvement within a month, and probably at least a three months' trial would be necessary in order to judge.

REFERENCE

1 *Brit. med. J.*, 1960, **1**, 1828.

Latent Syphilis

Q.—*A man aged 81 with aortic incompetence has been found to have positive W.R. and Kahn reactions. His three children are all about 50 years of age and apparently in good health. Should they be subjected to blood tests or is it justifiable to leave well alone? The mother died of cancer 22 years ago.*

A.—The three children should certainly be tested. Latent syphilis, congenital or acquired, can be present for many years and then become manifest with serious results. The tests should be done without disclosing the diagnosis in the case of the father, because to do so would probably cause great unhappiness to everyone concerned. There are many reasons for taking blood tests, and the story of a low-grade infection of long standing which occasionally affects other members of the family is usually acceptable.

Haemophilia in a Family

Q.—*A girl aged 20 is contemplating marriage. The family history is that her maternal grandfather suffered from haemophilia, but, in spite of this, had three sons, said to be normal, and three daughters. Of the sons' families, all the offspring appear normal, but of the daughters one has two sons who are both haemophiliacs, another has two daughters, and the third, my patient's mother, has also two sons with haemophilia. What are the chances of this girl producing a normal child who would not, in turn, pass on this inheritable disease?*

A.—This is a typical pedigree of a sex-linked recessive condition. Since the maternal grandfather had the gene for haemophilia on his X chromosome, all his sons, to whom he has transmitted his Y chromosome, will be unaffected and cannot have affected children. His daughters, to whom he has transmitted his X chromosome, are all carriers of the gene for haemophilia. The patient's mother is therefore a carrier of the gene, and this is confirmed by the fact that she has had two sons with haemophilia. The chance of the patient being a carrier like her mother is 1 in 2; the risks to her children are, therefore, for the boys 1 in 4 of having haemophilia, and for the girls 1 in 4 of being a carrier of haemophilia.

While, in general, carrier women cannot be identified by laboratory tests, such as estimations of the anti-haemophiliac globulin titre, there are families with mild haemophilia in which such tests are helpful in detecting carrier women,[1] and an expert haematological investigation of this family would be worth while.

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Congenital Dysplasia of the Hip

Q.—*How should one examine for and diagnose congenital dysplasia of the hip, especially in bilateral cases, in very young babies?*

A.—Congenital dysplasia of the hip in very young babies presents either as a partial displacement or as a complete dislocation Dysplasia should be suspected in babies with a family history of congenital dislocation of the hip. Asymmetric buttock creases and limitation of hip abduction warrant radiological examination—even in bilateral cases the buttock creases are usually asymmetric. It should be noted, however, that these clinical signs are not always accompanied by radiological evidence of displacement.

Ortolani[1] described a simple method for detecting congenital dislocation of the hip in the newborn—a click is felt when the leg is maximally turned outwards in maximal abduction. Arthrography confirms that the click occurs as the head snaps over the socket wall.

All suspected cases should be examined radiographically. (1) A shallow acetabular angle with no displacement of the upper end of the femur does not necessarily imply impending dislocation.[2] Such cases may be x-rayed again at 4 months, by which time the majority will have formed a normal acetabular angle. (2) Upward or lateral displacement of the upper end of the femur indicates definite subluxation or dislocation. The upper end of the femur should not lie above a line drawn through the upper margin of the symphysis.[3] (3) Dislocation of the hip in the newborn may be demonstrated radiographically by forcible abduction to at least 45° with appreciable inward rotation of the femora.[4] The head is forced either into or out of the socket. If dislocated, the line of the femur shaft will point above the upper edge of the bony acetabular wall. (4) Treatment of doubtful cases by simple abduction will restore stability within a few months.

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Correction.—We regret a printing error in the paper "A Freeze-dried Vaccine from Isoniazid-resistant B.C.G." (May 27, p. 1500) In Table II the percentage positive, with isoniazid, with batch 331 of the resistant vaccine should have been 100, not 104 as printed.

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